A 65-year-old man with a history of congestive heart failure is hospitalized with chest pain and hypotension requiring admission to the cardiac care unit. An intra-arterial line is placed for direct blood pressure monitoring. Consecutive readings of his intra-arterial blood pressure are 75, 110, 80, 90, 75, and 110 mm Hg. Which of the following represents the median of these blood pressure readings?

A. 80 mm Hg
B. 85 mm Hg
C. 90 mm Hg
D. 100 mm Hg
E. 110 mm Hg

Submit

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- A. 80 mm Hg (2%)
- ✓ B. 85 mm Hg (88%)
- C. 90 mm Hg (7%)
- D. 100 mm Hg (0%)
- E. 110 mm Hg (0%)

Omitted
Correct answer
B

88%
Answered correctly

09 mins, 10 secs
Time Spent

07/05/2020
Last Updated

Explanation

It is important to understand the difference between the median, mean, and mode, which are 3 measures of central tendency. The **median** of an ordered dataset is the number that separates the right half of the data from the left half. The dataset MUST be ordered before the median is determined. If the number of observations in the dataset is even, finding the median requires adding the middle 2 values together and dividing that sum by 2.

The ordered dataset in this case is {75, 75, **80, 90**, 110, 110}. There are 6 observations, which is an even number of observations. The median value splits the dataset in half; it lies between 80 and 90 (3 values on the left and 3 values on the right). The median is (80 + 90) / 2 = 85 mm Hg.

Now, assume one of the values is missing and the ordered dataset includes the following 5 observations (odd number of observations): {75, 80,

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B

Answered correctly Time Spent Last Updated

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Now, assume one of the values is missing and the ordered dataset includes the following 5 observations (odd number of observations): {75, 80, **90**, 110, 110}. In this case, the median value would be 90 mm Hg, which splits the dataset in half (2 values on the left and 2 values on the right).

(Choices A and D) The values 80 and 100 mm Hg are not measures of the center of the dataset.

(Choice C) To find the **mean** of a dataset, add all of the observations and divide that sum by the number of observations. In this case, the mean is (75 + 75 + 80 + 90 + 110 + 110) / 6 = 90 mm Hg.

(Choice E) Another measure of the center of a dataset is the mode. Finding the **mode** is easy because it is the most frequent value of a dataset. In our scenario, the dataset is "bimodal" because 75 and 110 mm Hg are each listed twice.

Educational objective:
The median is the value that is located in the precise center of an ordered dataset. It separates the right half of the data from the left half.

Biostatistics	Biostatistics & Epidemiology	Central tendency (mean, median, mode, outliers)
Subject	System	Topic

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A study is conducted to assess the relationship between smoking status and forced expiratory volume in one second (FEV_1). Subjects are randomly selected and categorized based on smoking status. Group A consists of 200 nonsmokers, group B consists of 200 light smokers (1-7 cigarettes per day), group C consists of 200 moderate smokers (8-22 cigarettes per day), and group D consists of 200 heavy smokers (23+ cigarettes per day). FEV_1 is quantitatively measured in all participants using properly calibrated office spirometers. Which of the following is the most appropriate statistical method to compare the mean FEV_1 results among all 4 groups?

A. Analysis of variance

B. Chi-square test

C. Meta-analysis

D. Multiple logistic regression

E. Pearson correlation coefficient

F. Two-sample *t*-test

Submit

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- ✓ A. Analysis of variance (63%)
- B. Chi-square test (21%)
- C. Meta-analysis (4%)
- D. Multiple logistic regression (2%)
- E. Pearson correlation coefficient (4%)
- F. Two-sample *t*-test (2%)

Omitted
Correct answer
A

63%
Answered correctly

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04/29/2020
Last Updated

Explanation

Analysis of variance (ANOVA)

Null hypothesis

Alternate hypothesis

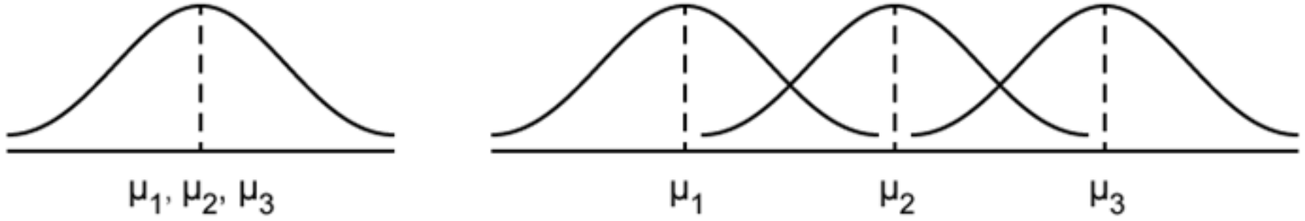
Analysis of variance (ANOVA)

Null hypothesis

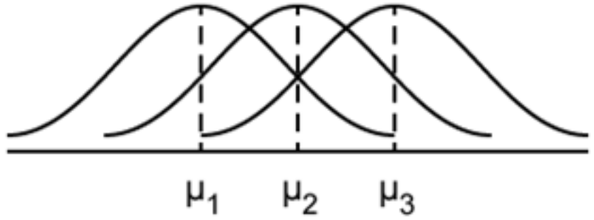
All samples drawn from the same population ($\mu_1=\mu_2=\mu_3$)

Alternate hypothesis

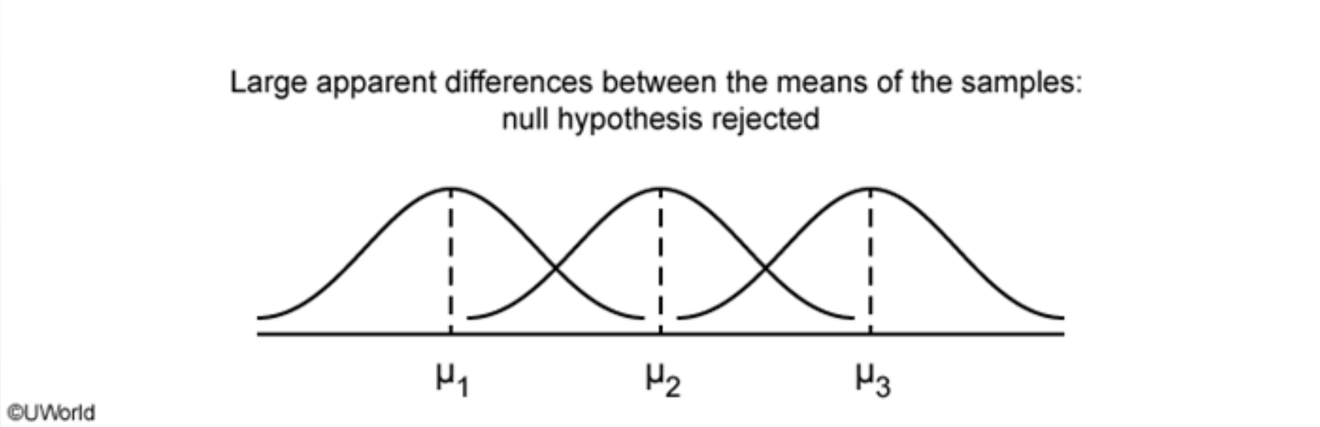
Samples drawn from different populations ($\mu_1\neq\mu_2\neq\mu_3$)



Small apparent differences between the means of the samples: null hypothesis not rejected



Large apparent differences between the means of the samples: null hypothesis rejected



Analysis of variance (ANOVA) is used to determine whether there are any significant **differences between the means** of **several independent groups**.

ANOVA compares the means between the groups relative to the variability within groups (F-test) and determines whether any of those means are significantly different from one another. Specifically, it tests the **null hypothesis** that all groups are simply random samples of the same population (ie, the **means are the same**). The null hypothesis is rejected when there are at least 2 group means that are significantly different from one another.

ANOVA can be used to compare ≥2 groups but is generally used to compare **≥3 groups** (because other equivalent methods exist to compare 2 groups). For example, the 2 independent samples *t*-test is a special case of the F-test in ANOVA. The assumptions for both tests and their resulting *p*-values are the same.

(Choice B) Chi-square tests can be used to evaluate the association between 2 *categorical* variables. For example, if FEV_1 is measured as a categorical variable (eg, normal or low), then a chi-square test could be used to determine if there is an association between FEV_1 and smoking status. However, this study is specifically comparing the mean FEV_1 results (a *quantitative* variable) between groups.

(Choice C) Meta-analysis involves the pooling of data from several studies to perform an analysis with greater statistical power than the individual studies alone. For example, individual studies assessing the effects of aspirin on certain cardiovascular events may be inconclusive. However, analysis of data compiled from multiple clinical trials may reveal a significant benefit.

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(Choice D) Multiple logistic regression is a method used to predict the probability of a binary outcome (eg, presence or absence of gastric cancer) based on 1 or more independent variables that can be either continuous or categorical. For example, this test could be used to predict the probability of gastric cancer based on alcohol consumption, tobacco use, and charred food consumption.

(Choice E) The Pearson correlation coefficient is a measure of the strength and direction of a linear relationship between 2 quantitative (ie, continuous) variables. For example, a study may report a correlation coefficient describing the association between hemoglobin A1c levels and average blood glucose levels.

(Choice F) A two-sample *t*-test can be used when 2 group means are compared. This test could have been used for the example in the question if the study participants were divided into smoking and nonsmoking groups only (ie, 2 groups instead of 4).

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Educational objective:
A *t*-test is used to compare the difference between the means of 2 groups. Analysis of variance (ANOVA) compares the difference between the means of 2 or more groups. Results from a *t*-test and ANOVA test will be equivalent when comparing the difference between the means of 2 groups.

Biostatistics	Biostatistics & Epidemiology	Statistical tests
Subject	System	Topic

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A suburban hospital is undergoing an annual review by a health care accreditation organization. As part of the process, iatrogenic infection rates are assessed for all major hospital services. Inpatient surgical infection statistics for the last year are shown below.

Surgical infection	Number of fatal cases	% of all fatal cases	Number of nonfatal cases	% of all nonfatal cases
Cl difficile	2	3	14	6
S aureus, methicillin-sensitive	10	13	25	11
S aureus, methicillin-resistant	40	53	70	32
E coli	10	13	50	23
Cl perfringens	1	1	1	<1
S epidermidis	2	3	30	14
Other	10	13	30	14
Total	**75**	**100**	**220**	**100**

What is the case-fatality rate for methicillin-resistant *S aureus* surgical infections in this hospital?

A. 40/70
B. 40/110
C. 40/75
D. 53/100
E. 70/220

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S epidermidis	2	3	30	14
Other	10	13	30	14
Total	**75**	**100**	**220**	**100**

What is the case-fatality rate for methicillin-resistant *S aureus* surgical infections in this hospital?

- A. 40/70 (6%)
- ✓ B. 40/110 (80%)
- C. 40/75 (9%)
- D. 53/100 (2%)
- E. 70/220 (0%)

Omitted
Correct answer

80%
Answered correctly

04 secs
Time Spent

05/07/2020
Last Updated

Omitted
Correct answer
B

80%
Answered correctly

04 secs
Time Spent

05/07/2020
Last Updated

Explanation

Case-fatality rate (CFR) is a measure of the **severity of a disease** or condition. It is defined as the **proportion** of reported cases of a specific disease or condition (eg, methicillin-resistant *S aureus*, [MRSA]) that are **fatal** within the population affected by the disease or condition over a specific time. The CFR can be calculated as the number of fatal cases of disease or condition divided by the total number of people with the disease or condition.

In this scenario, 40 fatal and 70 nonfatal cases of MRSA infection are reported. Therefore, the CFR is:

$$\text{CFR} = 40 / (40 + 70) = \mathbf{40 / 110}$$

(Choice A) This choice describes the ratio of fatal to nonfatal MRSA infection cases (40/70).

(Choices C and D) These choices describe the proportion of MRSA deaths out of all surgical infection deaths (40/75 = 53/100).

(Choice E) This choice describes the proportion of nonfatal cases of MRSA infection out of all nonfatal surgical infection cases (70/220).

Educational objective:
Case-fatality rate is calculated by dividing the number of fatal cases of a disease or condition by the total number of people with that disease or condition.

Subject	System	Topic
Biostatistics	Biostatistics & Epidemiology	Morbidity and mortality rates

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A large prospective study evaluates the relationship between alcohol consumption and breast cancer. A total of 4000 middle-aged women are enrolled in the study through a random selection of residential addresses. Daily alcohol consumption and breast cancer incidence are assessed through the use of periodic questionnaires. On five-year follow-up, the investigators report the association between alcohol consumption and breast cancer as a relative risk of 1.32 (95% confidence interval = 0.90-1.85); 800 subjects were lost to follow-up by the end of the study, the majority of whom were moderate to heavy alcohol consumers. According to this information, which of the following biases is most likely to be present and may have affected the results?

- A. Lead-time bias
- B. Observer bias
- C. Random misclassification bias
- D. Recall bias
- E. Selection bias

Submit

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- A. Lead-time bias (13%)
- B. Observer bias (6%)
- C. Random misclassification bias (11%)
- D. Recall bias (11%)
- ✓ E. Selection bias (56%)

Omitted
Correct answer
E

56%
Answered correctly

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Explanation

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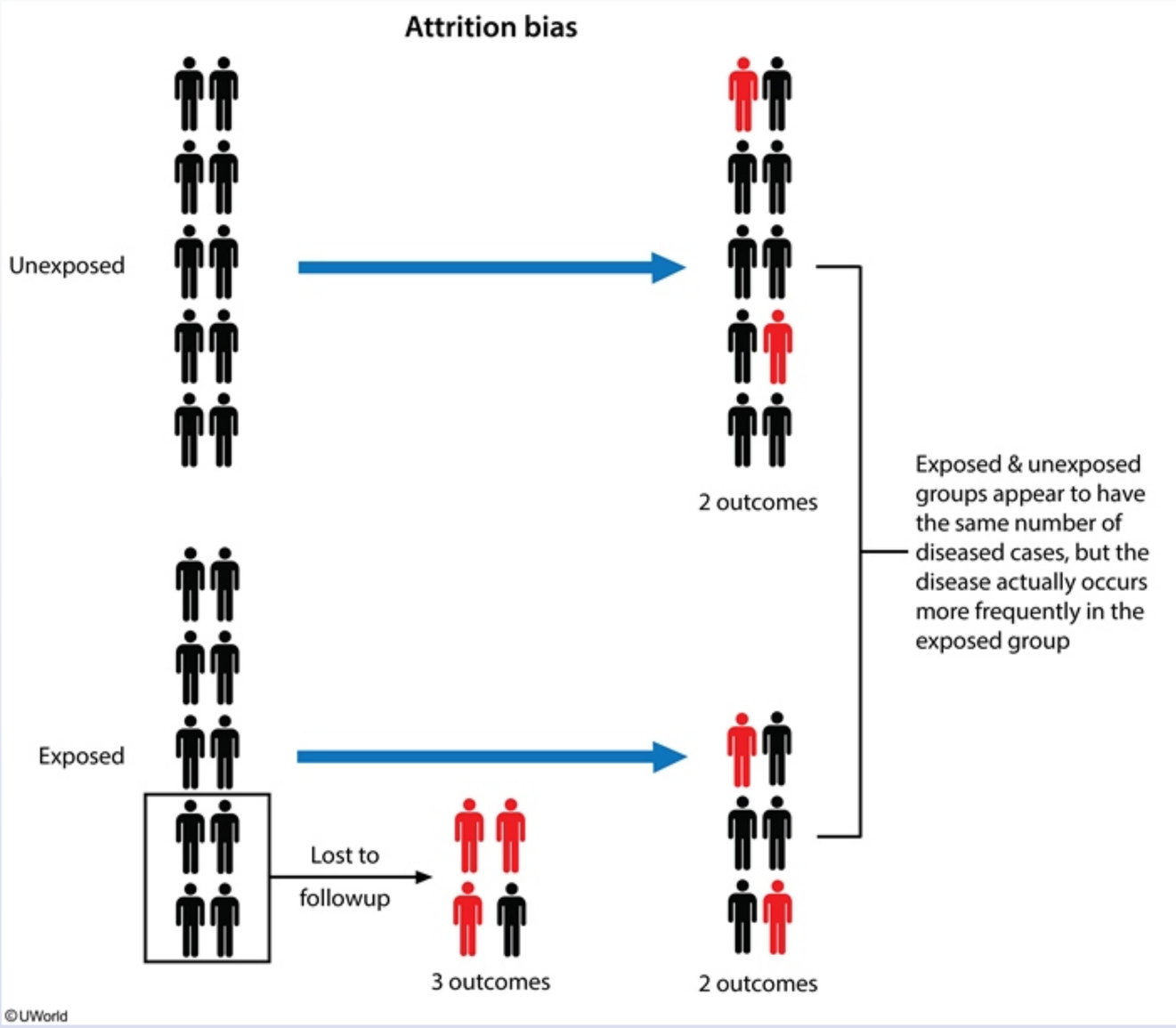

3 outcomes 2 outcomes

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Bias refers to a systematic error (due to nonrandom factors) that can result in an incorrect association between the exposure and outcome. In general, when bias is present, the results are consistently distorted in one direction. In prospective studies, if loss to follow-up occurs disproportionately between the exposed and unexposed groups, **attrition bias** can result if the lost subjects differ in their risk of developing the outcome compared to the remaining subjects. Attrition bias is a form of **selection bias** (a term that most often refers to systematic differences between groups in terms of treatment response or prognosis). Attrition bias does not occur when the losses happen randomly between the exposed and unexposed groups, as this simply leads to a smaller study population.

In this example, a substantial number of subjects (800 / 4000 = 20%) were lost to follow-up, primarily those with higher levels of alcohol consumption. If these lost subjects had a higher incidence of breast cancer than those remaining in the study, then a selective loss of high-risk subjects would have occurred in the exposed group. As a result, the measure of the association between alcohol use and breast cancer would be underestimated, which might explain why no significant association was seen in this study (as the confidence interval of 0.90 to 1.85 crosses 1, which is the null value for relative risk).

(Choice A) Lead-time bias occurs when a screening test diagnoses a disease earlier than it would have appeared by natural history alone, so that the time from diagnosis until death appears prolonged even though there might actually be no improvement in survival.

(Choice B) Observer bias can occur in clinical trials when study participants or investigators are aware of individual treatment assignments. It can be prevented by performing a double-blind study in which neither participants nor investigators are aware of treatment assignments.

(Choice C) Misclassification bias occurs when either the exposure or the outcome is not identified correctly. Random (or nondifferential) misclassification affects all groups to the same extent. For example, if a pediatric size sphygmomanometer cuff is used on all participants (treatment and control groups) as part of a study in adult patients, the blood pressure readings will be incorrect (due to the incorrect cuff size). However, the resulting misclassification will likely affect both groups to the same extent (because the same cuff was used).

(Choice D) Recall bias results from the inaccurate recall of past exposure status. It is a potential problem for retrospective studies such as case-control studies, particularly when questionnaires are used to inquire about distant past exposure. However, in this prospective study, exposure status is determined through periodic questionnaires assessing daily alcohol consumption (without inquiring about distant past exposure). In such a scenario, recall bias is less likely to affect results.

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Educational objective:
In prospective studies, disproportionate loss to follow-up between the exposed and unexposed groups creates the potential for attrition bias, which is a form of selection bias. As a result, investigators generally try to achieve high patient follow-up rates in prospective studies.

Biostatistics	Biostatistics & Epidemiology	Confounding, effect modification, bias, errors
Subject	System	Topic

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Researchers are studying the relationship between essential hypertension and a common mutation in the structure of a sodium channel protein. A study population is randomly selected and blood samples are obtained for leukocyte genotyping. The prevalence of hypertension is determined based on mean blood pressure measurements obtained using standardized ambulatory blood pressure monitoring conducted over 1 week. Based on the analysis results, the researchers conclude that the sodium channel structure mutation is associated with hypertension. Which of the following best describes the study design used by the investigators?

A. Case-control study

B. Cross-sectional study

C. Prospective cohort study

D. Randomized clinical trial

E. Retrospective cohort study

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A. Case-control study (10%)
✓ B. Cross-sectional study (56%)
C. Prospective cohort study (17%)
D. Randomized clinical trial (9%)
E. Retrospective cohort study (6%)

Omitted
Correct answer
B

56%
Answered correctly

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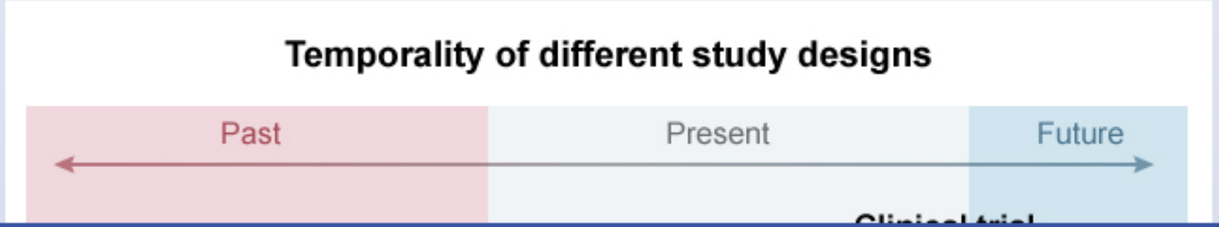
Last Updated

Explanation



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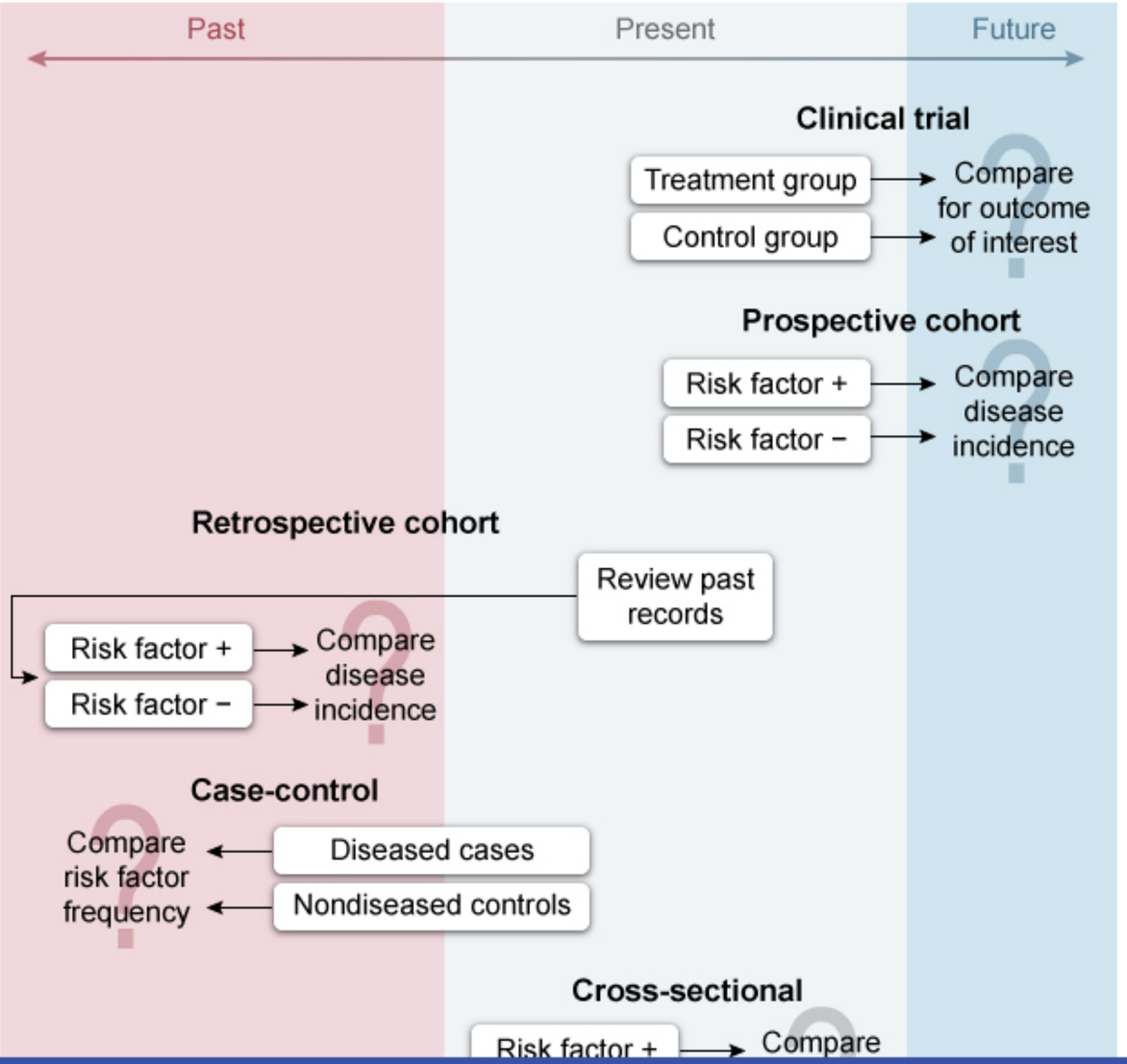
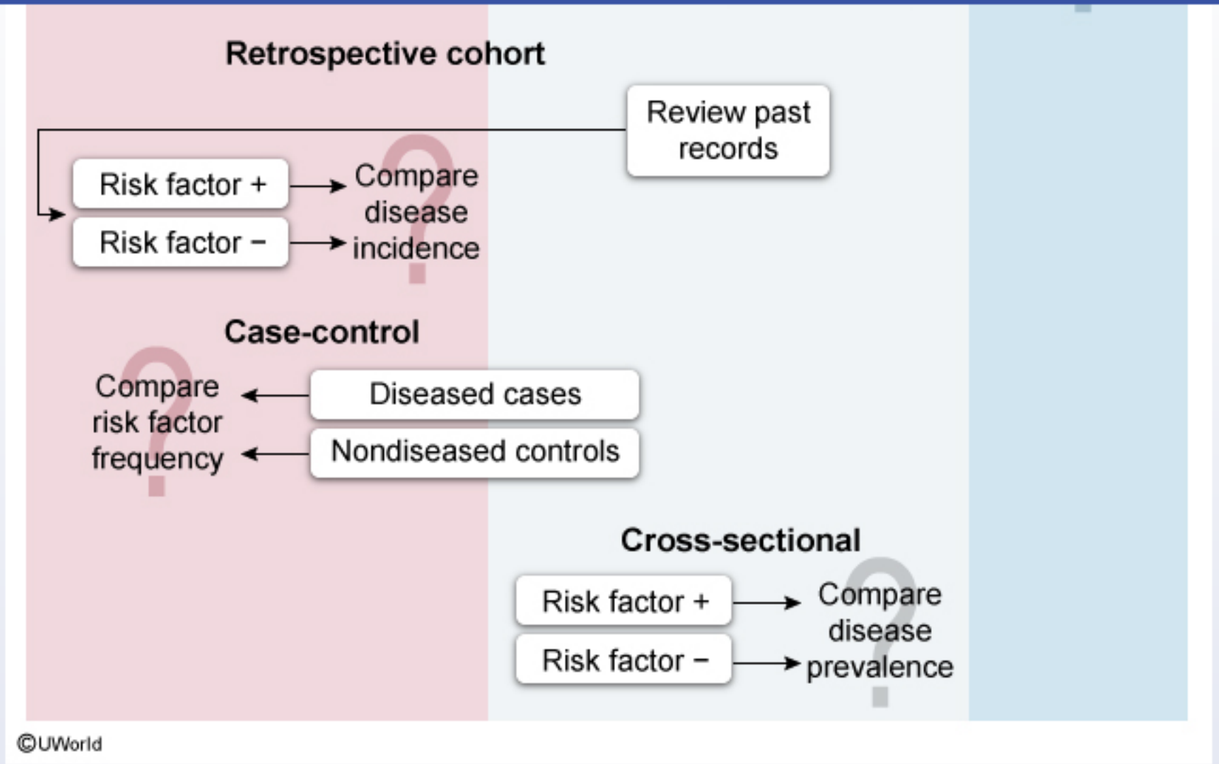
Temporality of different study designs





A **cross-sectional** study (also known as a prevalence study) simultaneously measures exposures and outcomes. The cross-sectional study has a "**snapshot**" design that is frequently used in surveys, mostly because it is inexpensive and easy to perform. In this example, a snapshot was obtained of individuals randomly selected from the population; their blood samples were analyzed for the presence of the sodium channel protein mutation and the prevalence of hypertension was calculated. The subjects' blood pressure was measured over 7 days to obtain an average measurement (likely to limit the results being impacted by white-coat hypertension and other transient causes of hypertension). The major limitation of a cross-sectional study design is that a temporal relationship between exposure and outcome is not always clear. However, in this case, demonstrating a temporal relationship was straightforward because the possession of a specific genotype clearly precedes hypertension.

(Choice A) A case-control study is designed by selecting individuals with a particular disease (cases), individuals without that disease (controls), and then evaluating previous exposure status. This study would have been classified as a case-control study if it had explicitly recruited individuals with (cases) and without (controls) hypertension (rather than randomly selecting a sample from a population) and evaluated their

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(Choices C and E) A prospective cohort study would have taken individuals without hypertension from the population, analyzed their blood samples to determine the distribution of the sodium channel mutation, and followed them over time (years) to determine the proportion of new cases of hypertension in patients with and without the mutation. In this example, although hypertension was measured over several days, the objective was not to document incidence of new cases of hypertension (which would be unlikely to develop over 1 week) but to measure the prevalence of hypertension while ensuring that average blood pressure measurements were obtained.

A retrospective design would have also assessed incidence (not prevalence) of hypertension compared to an earlier period of time, based on a chart review of historic data. Prospective and retrospective cohort studies are organized by selecting a group of individuals (ie, a cohort) who do **not** have the disease of interest (eg, hypertension), determining their exposure status, and then following them (forward in time or from a point in the past to the present) to assess for the development of the disease.

(Choice D) A randomized clinical trial directly compares ≥2 treatments. Usually, the subjects are randomly assigned to experience a specific exposure (eg, a medication) or no exposure (eg, placebo) and are then followed to assess for the outcome of interest (eg, disease).

Educational objective:
In a cross-sectional study, exposure and outcome are measured simultaneously at a particular point in time ("snapshot study"). In other study designs, a certain time period separates the exposure from the outcome.

limitation of a cross-sectional study design is that a temporal relationship between exposure and outcome is not always clear. However, in this case, demonstrating a temporal relationship was straightforward because the possession of a specific genotype clearly precedes hypertension.

(Choice A) A case-control study is designed by selecting individuals with a particular disease (cases), individuals without that disease (controls), and then evaluating previous exposure status. This study would have been classified as a case-control study if it had explicitly recruited individuals with (cases) and without (controls) hypertension (rather than randomly selecting a sample from a population) and evaluated their sodium channel mutation patterns.

(Choices C and E) A prospective cohort study would have taken individuals without hypertension from the population, analyzed their blood samples to determine the distribution of the sodium channel mutation, and followed them over time (years) to determine the proportion of new cases of hypertension in patients with and without the mutation. In this example, although hypertension was measured over several days, the objective was not to document incidence of new cases of hypertension (which would be unlikely to develop over 1 week) but to measure the prevalence of hypertension while ensuring that average blood pressure measurements were obtained.

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Educational objective:
In a cross-sectional study, exposure and outcome are measured simultaneously at a particular point in time ("snapshot study"). In other study designs, a certain time period separates the exposure from the outcome.

Biostatistics	Biostatistics & Epidemiology	Study designs
Subject	System	Topic

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A 34-year-old man is admitted to the hospital with acute chest pain. An ECG is obtained in the emergency department and shows ST segment elevation in leads II, III, and aVF. A sample of blood is taken from the patient, and a new test is used to measure plasma homocysteine levels. The test is repeated 3 times with his blood sample, and the results are 11.8 μmol/L, 9.2 μmol/L, and 13.7 μmol/L (laboratory reference range: 4-14). Which of the following parameters is most likely to be low based on the results of the new test?

A. Accuracy
B. Precision
C. Sensitivity
D. Specificity
E. Validity

Submit

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- A. Accuracy (12%)
- ✓ B. Precision (79%)
- C. Sensitivity (2%)
- D. Specificity (2%)
- E. Validity (3%)

Omitted
Correct answer
B

79%
Answered correctly

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01/19/2020
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Explanation

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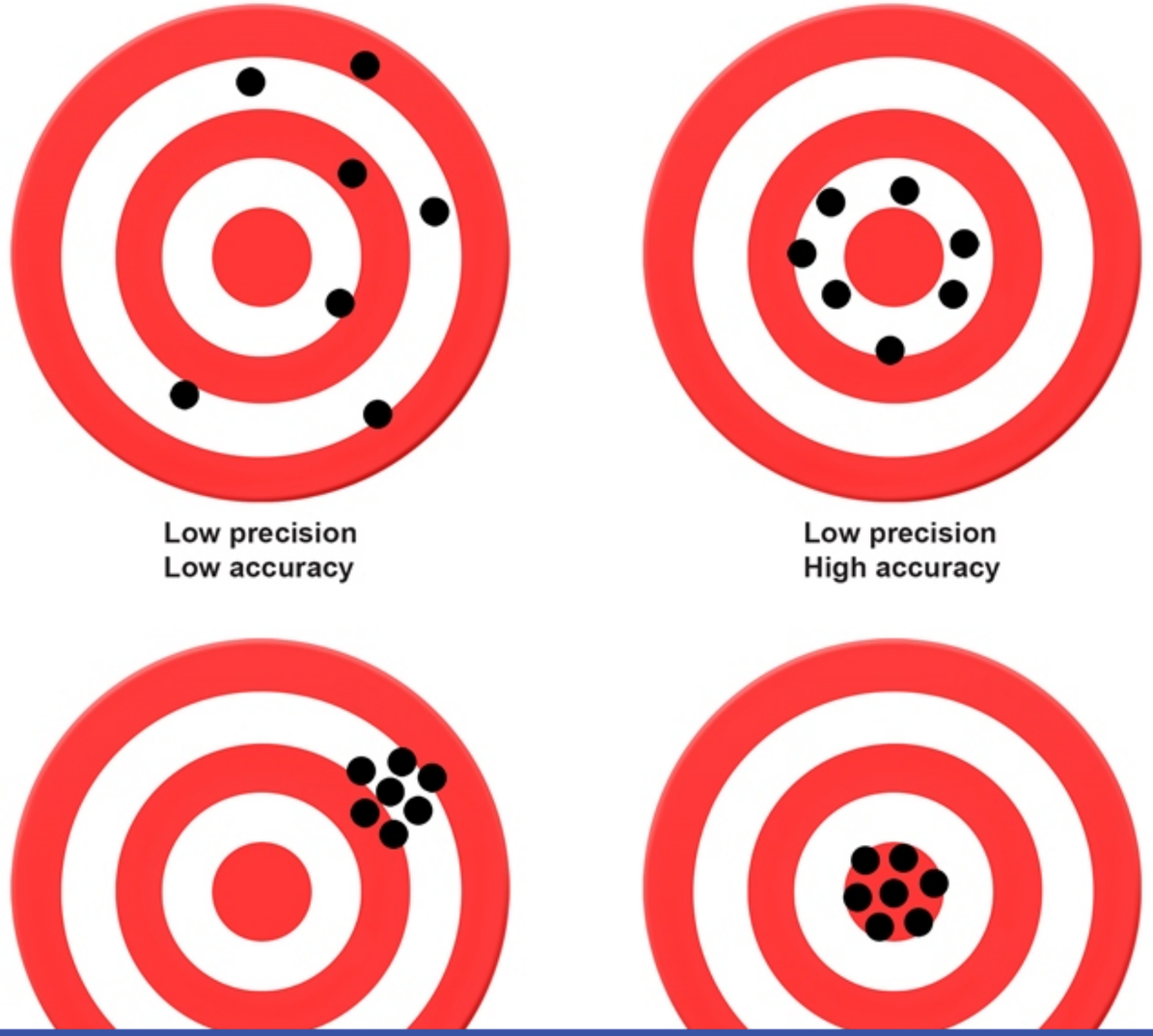
Precision & accuracy



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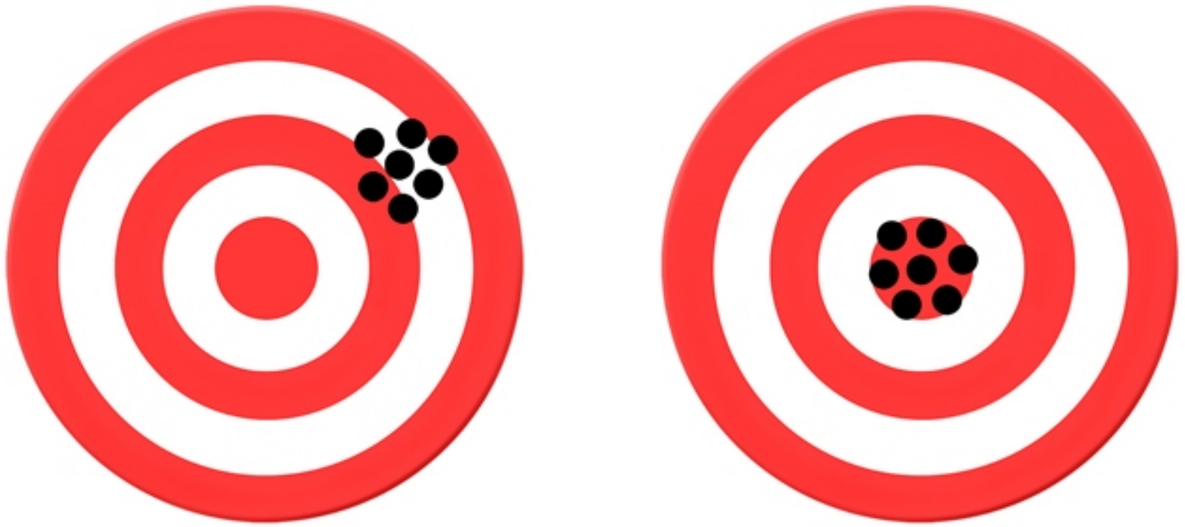

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A measurement tool should be precise and accurate to be useful in the clinical setting. Precision and accuracy are defined as follows:

- **Precision** (reliability) is the ability of a test to reproduce identical or similar results with repeated measurements (bottom half of figure).
- **Accuracy** (validity) is the ability of a test to measure what it is supposed to measure. For a new test to be accurate, its results should be equivalent to the results obtained with a "gold standard" (eg, best conventional test available) on the same individual (right half of figure).

A precise test gives similar or very close results on repeat measurements. In this example, repeat measurements of the same sample yielded different results; therefore, the new test has low precision.

(Choices A and E) To evaluate the accuracy of a new test, its results should be compared to those obtained with the gold standard test on the same individual. A test can be highly precise (ie, gives very similar results on repeat measurements) but inaccurate (ie, the measurements are all incorrect compared to the gold standard). A test that is highly imprecise is also highly inaccurate. In this case, as there were no test results obtained using the "gold standard", the accuracy/validity of the test cannot be determined.

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(Choices C and D) Sensitivity is defined as a test's ability to identify the true presence of disease, whereas specificity is defined as a test's ability to identify the true absence of disease. Poor reliability can limit the sensitivity or specificity of a test if the results from healthy and diseased populations are close in value.

Educational objective:
A precise/reliable test is reproducible in that it gives similar results on repeat measurements. Reliability is maximal when random error is minimal.

Biostatistics	Biostatistics & Epidemiology	Validity And Reliability
Subject	System	Topic

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A researcher is interested in assessing the blood folate level of women who live in a population with a high incidence of neural tube defects. She takes a large random sample (n) of women age 18-45 and measures their blood folate levels. The researcher finds that the data are normally distributed, and she reports the mean and standard deviation (SD) of the sample. To account for sampling variation, she decides to calculate a 95% confidence interval to estimate the mean of the entire population. The researcher concludes that 2.4 to 4.6 ng/mL might be a likely range for the true, unknown population mean. Which of the following calculations was most likely used to compute this interval estimate of the population mean?

A. Mean ± 1.96 × SD

B. Mean ± 1.96 × (SD/$\sqrt{n}$)

C. Mean ± 2.58 × SD

D. Mean ± 2.58 × (SD/$\sqrt{n}$)

E. Mean ± (SD/n)

Submit

A researcher is interested in assessing the blood folate level of women who live in a population with a high incidence of neural tube defects. She takes a large random sample (*n*) of women age 18-45 and measures their blood folate levels. The researcher finds that the data are normally distributed, and she reports the mean and standard deviation (SD) of the sample. To account for sampling variation, she decides to calculate a 95% confidence interval to estimate the mean of the entire population. The researcher concludes that 2.4 to 4.6 ng/mL might be a likely range for the true, unknown population mean. Which of the following calculations was most likely used to compute this interval estimate of the population mean?

A. Mean ± 1.96 × SD (18%)

✓ B. Mean ± 1.96 × (SD/√*n*) (63%)

C. Mean ± 2.58 × SD (4%)

D. Mean ± 2.58 × (SD/√*n*) (8%)

E. Mean ± (SD/*n*) (5%)

Omitted
Correct answer
B

63%
Answered correctly

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05/05/2020
Last Updated

Explanation

The **normal distribution** is a continuous distribution that follows a bell-shaped curve with a single peak at the mean value. One of the most important properties of the normal distribution is its **symmetry** about its mean, which allows for determination of the percentage of all observations that lie within 1, 2, or 3 standard deviations (SDs). The "68/95/99 rule" states that 68% of all observations lie within 1 SD of the mean, 95% within 2 SDs of the mean, and 99.7% within 3 SDs of the mean. These are helpful approximations; however, when considering the normal distribution,

The **normal distribution** is a continuous distribution that follows a bell-shaped curve with a single peak at the mean value. One of the most important properties of the normal distribution is its **symmetry** about its mean, which allows for determination of the percentage of all observations that lie within 1, 2, or 3 standard deviations (SDs). The "68/95/99 rule" states that 68% of all observations lie within 1 SD of the mean, 95% within 2 SDs of the mean, and 99.7% within 3 SDs of the mean. These are helpful approximations; however, when considering the normal distribution, exactly **95% of the observations** lie within **1.96 SDs** of the mean and 99% of the observations lie within 2.58 SDs (1.96 and 2.58 represent *z*-scores for 95% and 99% of the distribution, respectively).

Most research is done using **samples** rather than entire populations. This introduces some variability when calculating population parameters such as mean value (eg, when different samples are drawn from the same population, the means from all possible samples will often be slightly different). The **variability between sample means** can be calculated in a way analogous to calculating the SD of a group of observations in a single sample. The "standard deviation" of a series of sample means is known as the **standard error** (**SE**) of the mean, and it estimates how far the sample mean is likely to be from the unknown population mean. The SE is estimated considering both the SD and the size of the sample (*n*) in the following manner: **SD/√*n***.

A sample mean is a point estimate of the true population mean; however, a **confidence interval** (**CI**) better accounts for the variability due to sampling by including the SE in its calculation. The CI of the mean can be calculated as follows:

$$\text{CI of mean} = \text{mean} \pm [\text{z-score for confidence level}] \times [\text{SE}]$$

where the *z*-score for confidence level represents the number of SEs containing the desired percentage of observations around the mean (eg, 95%, 99%). In this case, the 95% CI can be calculated:

$$\text{CI of mean} = \textbf{mean} \pm 1.96 \times (\text{SD}/\sqrt{n})$$

The sample size and the SD of the sample determine the magnitude of the variability due to sampling. As *n* increases, SE decreases, and the CI becomes narrower and more precise. Conversely, as the SD increases, SE increases, and the CI becomes wider and less precise.

(Choice A) CI estimates use the SE of the mean, which takes into account the SD and the size of the sample (*n*). As such, the equation divides the SD by the square root of *n*.

(Choices C, D, and E) As noted, the SD reflects the spread of individual values in a normal distribution. Multiplying the SD by a specific constant (*z*-score) gives us a range of values that encompass a certain proportion of the observations. The mean ± 1 × SD would cover 68% of the

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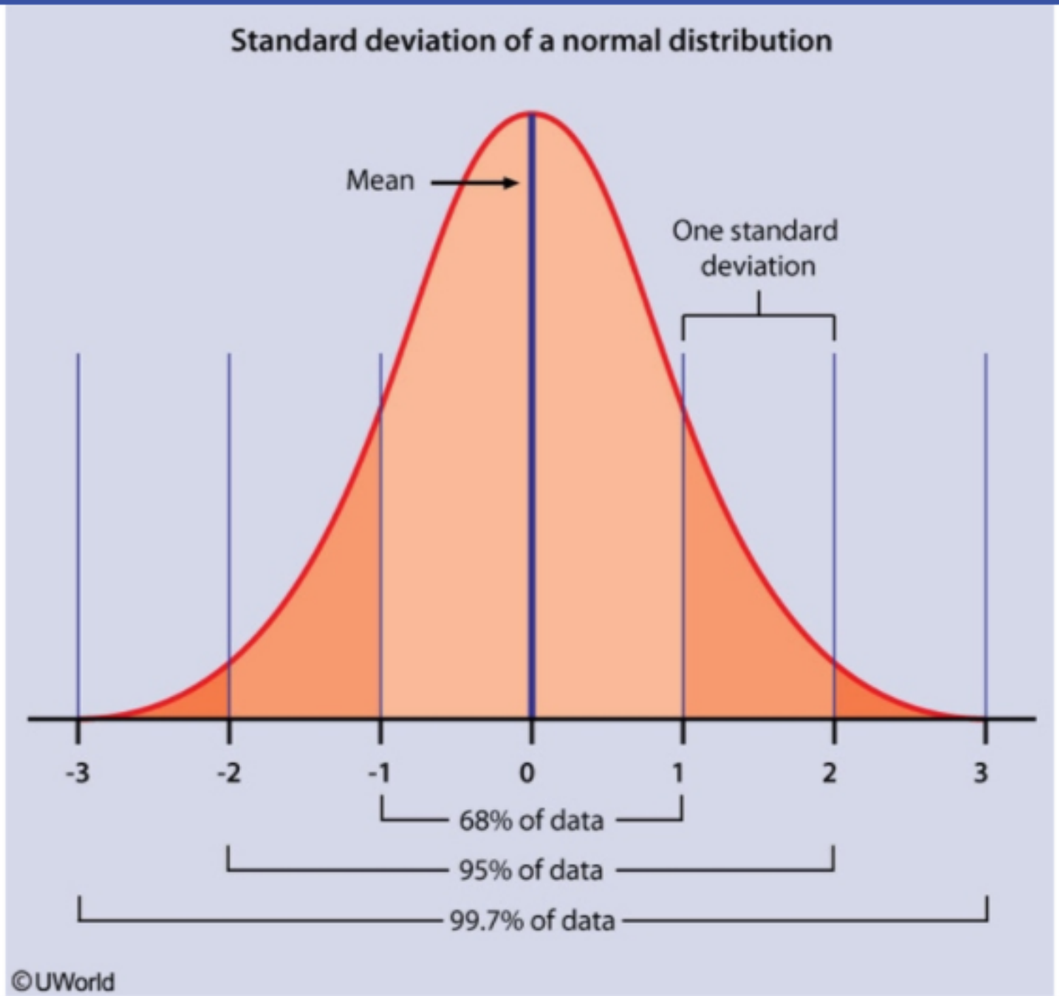

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CI of mean = mean ± [*z*-score for confidence level] × [SE]

where the *z*-score for confidence level represents the number of SEs containing the desired percentage of observations around the mean (eg, 95%, 99%). In this case, the 95% CI can be calculated:

CI of mean = **mean ± 1.96 × (SD/√*n*)**

The sample size and the SD of the sample determine the magnitude of the variability due to sampling. As *n* increases, SE decreases, and the CI becomes narrower and more precise. Conversely, as the SD increases, SE increases, and the CI becomes wider and less precise.

(Choice A) CI estimates use the SE of the mean, which takes into account the SD and the size of the sample (*n*). As such, the equation divides the SD by the square root of *n*.

(Choices C, D, and E) As noted, the SD reflects the spread of individual values in a normal distribution. Multiplying the SD by a specific constant (*z*-score) gives us a range of values that encompass a certain proportion of the observations. The mean ± 1 × SD would cover 68% of the observations, and the mean ± 2.58 × SD would cover 99% of the observations. However, the question is asking for a 95% CI, so the equation should use a *z*-score of 1.96 and the SE (ie, SD/√*n*).

Educational objective:
The standard deviation reflects the spread of individual values in a normal distribution (ie, it measures the variability of the observations within a single sample). The standard error of the mean reflects the variability of means (ie, variance between the means of different samples) and helps estimate the true mean of the underlying population.

Biostatistics	Biostatistics & Epidemiology	P-value and confidence interval
Subject	System	Topic

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A 62-year-old man with diabetes, hypertension, and hyperlipidemia comes to the emergency department of an academic medical center with chest pain, nausea, vomiting, and diaphoresis. An electrocardiogram demonstrates ST elevation in the anterior leads, and cardiac enzymes are markedly elevated. Investigators at the center are designing a randomized control trial to test the hypothesis that drug B will decrease the mortality associated with acute ST-elevation myocardial infarction compared to standard of care. To ensure that investigators will not miss a difference between drug B and standard of care (if a difference truly exists), which of the following would they want to maximize?

A. α

B. β

C. Type I error

D. Type II error

E. $1 - \beta$

Submit

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A. α (6%)

B. β (9%)

C. Type I error (6%)

D. Type II error (5%)

✓ E. 1 – β (72%)

Omitted
Correct answer
E

72%
Answered correctly

02 secs
Time Spent

02/01/2020
Last Updated

Explanation

Statistical **power**, (1 – β), represents a study's ability to detect a difference when one exists. It is the probability of rejecting the null hypothesis when it is truly false - ie, the probability of finding a true relationship. Power depends on sample size and the difference in outcome between the groups being tested. In this study, the researchers want to detect a difference between drug B and standard of care if one exists; they want to maximize power.

β is the probability of committing a type II error **(Choices B and D)**. Type II error occurs when researchers fail to reject the null hypothesis when it

Explanation

Statistical **power**, (1 – β), represents a study's ability to detect a difference when one exists. It is the probability of rejecting the null hypothesis when it is truly false - ie, the probability of finding a true relationship. Power depends on sample size and the difference in outcome between the groups being tested. In this study, the researchers want to detect a difference between drug B and standard of care if one exists; they want to maximize power.

β is the probability of committing a type II error **(Choices B and D)**. Type II error occurs when researchers fail to reject the null hypothesis when it is truly false. This causes investigators to miss true relationships. An example of a type II error would be a study finding that aspirin does not affect platelet function when, in fact, it does. Therefore, if β is set at 0.2, the power will be (1 – β) = 80%; there will be an 80% chance of rejecting the null hypothesis when it is truly false.

(Choices A and C) Type I error occurs when researchers reject the null hypothesis when the null hypothesis is really true. That is, a study finds a statistically significant difference between 2 groups when one does not truly exist. An example would be if a study concluded that candy improves heart failure mortality when, in fact, it does not. α is the maximum probability of making a type I error that a researcher is willing to accept. Generally, α is compared to the p-value, the probability of observing a given result (or more extreme) due to chance alone assuming the null hypothesis is true (eg, if there is no real difference between the groups). The value of α is typically set at 0.05, meaning that researchers are willing to accept up to a 5% chance of making a type I error. In such a scenario, if $p < 0.05$, the result is said to be statistically significant.

Educational objective:
Power (1 − β) is the probability of rejecting a null hypothesis when it is truly false. It is typically set at 80% and depends on sample size and difference between outcomes.

Biostatistics	Biostatistics & Epidemiology	Power and sample size
Subject	System	Topic

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Researchers studying the effects of hormone replacement therapy (HRT) on the risk of myocardial infarction (MI) among postmenopausal women calculate the relative risk (RR) of MI to be 1.30 ($p = 0.07$) among women who are taking HRT compared to those who are not. The researchers conclude that there is no statistically significant increased risk of MI with HRT (based on a cutoff of $\alpha = 0.05$). Subsequently, the results of a meta-analysis determine that there actually is an increased risk of MI, with an overall RR = 1.32 ($p = 0.03$) among postmenopausal women who are taking HRT compared to those who are not. Which of the following was the most likely problem in the first study?

A. Berkson's bias

B. Placebo effect

C. Poor blinding

D. Researcher expectancy

E. Sample size

Submit

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- A. Berkson's bias (7%)
- B. Placebo effect (1%)
- C. Poor blinding (3%)
- D. Researcher expectancy (9%)
- ✓ E. Sample size (77%)

Omitted
Correct answer
E

77%
Answered correctly

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Explanation

Type I (α) and type II (β) errors

	True status	
	There is a true	There is NO true

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Explanation

Type I (α) and type II (β) errors

		True status	
		There is a true difference (ie, H_0 is false)	**There is NO true difference** (ie, H_0 is true)
Study result	**Difference calculated as statistically significant** (ie, reject H_0)	**Correctly** conclude there is a difference	**Type I (α) error** (Falsely conclude there is a difference)
	Difference calculated as NOT statistically significant (ie, fail to reject H_0)	**Type II (β) error** (Falsely conclude there is NO difference)	**Correctly** conclude there is NO difference

H_0 = null hypothesis of no difference.

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The first study and the meta-analysis (combined results of several studies) had similar outcomes in terms of relative risk (RR); however, they arrived at different conclusions because the p-value reached statistical significance ($p < \alpha = 0.05$) in the meta-analysis but not in the first study. The most probable reason behind this is that the **larger** meta-analysis reflects the true status (increased risk of myocardial infarction [MI] with hormone replacement therapy [HRT]), whereas the first study result represented a **type II (β) error (falsely** concluded there was **no** increased risk

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The probability of a type II (β) error is related to how much **power** a study has to detect a difference when a difference actually exists (power = 1 – β). **Sample size** and power are related in that studies with a larger sample size have greater power to detect differences if these exist. The small sample size of the first study made it underpowered to detect a difference in outcome between patients who were treated with HRT and those who were not.

The sample size did not change the value of α (typically set at 0.05). However, because the first study was underpowered, the p-value obtained was not statistically significant ($p = 0.07 > \alpha = 0.05$), leading to a false conclusion of no increased risk of MI with HRT.

(Choice A) Berkson's bias refers to selection bias that can be created by selecting hospitalized patients as the control group.

(Choice B) Placebo effect refers to patients' expectations affecting an outcome. However, in this case, the control group is taking neither HRT nor a placebo medication.

(Choices C and D) Given that the RR obtained in the first study was similar to the one obtained in the meta-analysis (1.32 versus 1.30), it is unlikely that design flaws (eg, poor blinding, researcher expectancy) were present in the study.

Educational objective:
A study's power increases as its sample size increases. Therefore, the larger the sample, the greater the ability of a study to detect a difference when one truly exists.

Biostatistics	Biostatistics & Epidemiology	Power and sample size
Subject	System	Topic

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A new biomarker has been shown to allow for the early detection of non-small cell lung carcinoma. A preliminary analysis on a cohort study of this new test demonstrates that its use prolongs survival of lung cancer patients by 3 months when compared to the survival of patients diagnosed by conventional methods. A secondary analysis reveals no difference in 6-month mortality rates between the 2 groups. Which of the following factors most likely explains the study results?

A. Confounding
B. Lead-time bias
C. Length-time bias
D. Measurement bias
E. Observer bias
F. Rare disease assumption

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A. Confounding (1%)
✓ B. Lead-time bias (84%)
C. Length-time bias (11%)
D. Measurement bias (1%)
E. Observer bias (0%)
F. Rare disease assumption (0%)

Omitted
Correct answer
B

84%
Answered correctly

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05/07/2020
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Explanation

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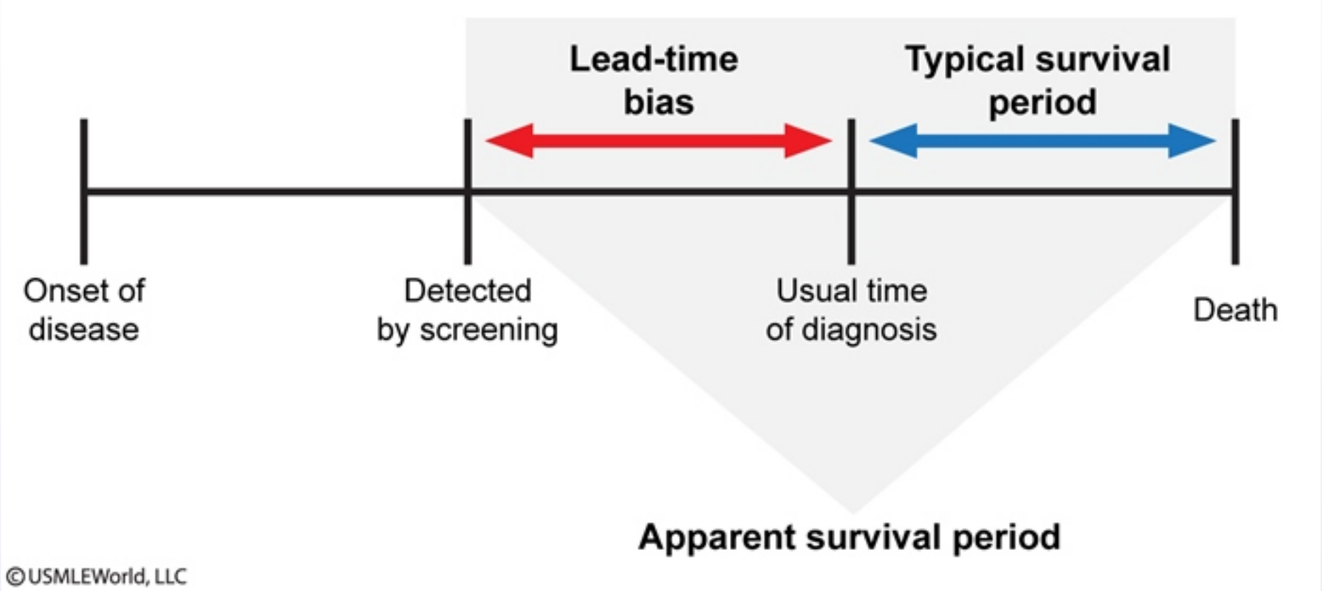

Lead-time bias should always be considered when evaluating any screening test. Lead-time bias is an **apparent increase in survival time** among patients undergoing screening when they actually have an **unchanged prognosis**. Patients screened with more sensitive tests may appear to live longer only because the disease was detected earlier than had it been diagnosed clinically. The overall length of time from disease onset to death actually remains the same with or without the earlier screening. To determine the actual effectiveness of the screening program, it is necessary to follow up patients for periods that are **longer** than the apparent increase in survival time, and then to estimate and compare mortality rates among patients who have undergone the additional screening and those who have not.

In this case, patients screened by the new test appeared to have increased their survival time by 3 months when compared to those diagnosed by conventional methods. However, there was **no difference in 6-month mortality** rate between the 2 groups, which indicates that there is no actual benefit to the screening program.

(Choice A) Confounding distorts the relationship between risk factors and the disease of interest, and can wholly or partially account for the observed effect. Although the results of this study could be potentially confounded, there is no information on how potential confounders were treated during the design or analysis stage of the study.

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Lead-time bias should always be considered when evaluating any screening test. Lead-time bias is an **apparent increase in survival time** among patients undergoing screening when they actually have an **unchanged prognosis**. Patients screened with more sensitive tests may appear to live longer only because the disease was detected earlier than had it been diagnosed clinically. The overall length of time from disease onset to death actually remains the same with or without the earlier screening. To determine the actual effectiveness of the screening program, it is necessary to follow up patients for periods that are **longer** than the apparent increase in survival time, and then to estimate and compare mortality rates among patients who have undergone the additional screening and those who have not.

In this case, patients screened by the new test appeared to have increased their survival time by 3 months when compared to those diagnosed by conventional methods. However, there was **no difference in 6-month mortality** rate between the 2 groups, which indicates that there is no actual benefit to the screening program.

(Choice A) Confounding distorts the relationship between risk factors and the disease of interest, and can wholly or partially account for the observed effect. Although the results of this study could be potentially confounded, there is no information on how potential confounders were treated during the design or analysis stage of the study.

(Choice C) Length-time bias occurs when subjects with a rapidly progressive form of disease are less likely to be detected by screening compared to those with slowly progressive disease. This bias tends to overstate the beneficial effects of screening on length of survival and mortality. In this case, there is no indication that the patients identified by the new test have more benign forms of lung cancer.

(Choices D and E) Measurement bias and observer bias refer to the misclassification of outcome and/or exposure (eg, labeling diseased as non-diseased and vice versa) and are related to poor study design. The scenario described does not mention how the study was conducted.

(Choice F) Rare disease assumption refers to the practice of approximating the odds ratio and relative risk when conducting a case-control study for rare diseases. According to the assumption, the odds ratio approximates relative risk when disease incidence is low (eg, <10%).

Educational objective:
Lead-time bias occurs when a new test diagnoses a condition earlier than conventional studies, causing an apparent increase in survival time despite no improvement in overall mortality. Long-term mortality rates, not survival times, should be considered for measuring the effect of early screening and treatment.

among patients undergoing screening when they actually have an **unchanged prognosis**. Patients screened with more sensitive tests may

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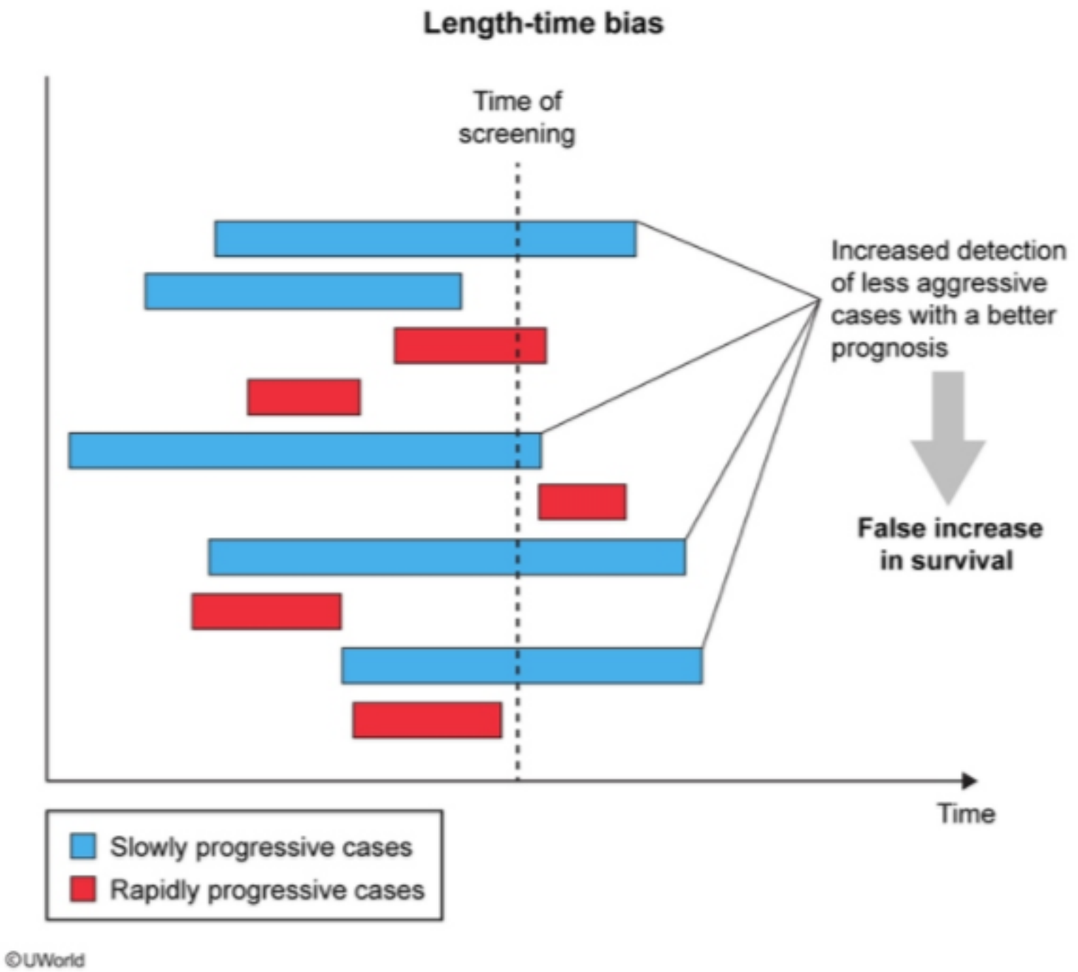

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Subject System Topic

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Researchers are developing an enzyme-linked immunosorbent assay test for diagnosing rheumatoid arthritis. The test is designed to detect the presence of serum antibodies against citrullinated proteins. Two test populations with a differing prevalence of rheumatoid arthritis are selected. The researchers plan to assess the test's performance in the 2 populations by comparing a number of diagnostic test parameters. Which of the following performance measures is most likely to be different between the 2 test populations?

A. Negative likelihood ratio

B. Positive likelihood ratio

C. Positive predictive value

D. Sensitivity

E. Specificity

Submit

Researchers are developing an enzyme-linked immunosorbent assay test for diagnosing rheumatoid arthritis. The test is designed to detect the presence of serum antibodies against citrullinated proteins. Two test populations with a differing prevalence of rheumatoid arthritis are selected. The researchers plan to assess the test's performance in the 2 populations by comparing a number of diagnostic test parameters. Which of the following performance measures is most likely to be different between the 2 test populations?

- A. Negative likelihood ratio (1%)
- B. Positive likelihood ratio (8%)
- ✓ C. Positive predictive value (80%)
- D. Sensitivity (6%)
- E. Specificity (3%)

Omitted
Correct answer
C

80%
Answered correctly

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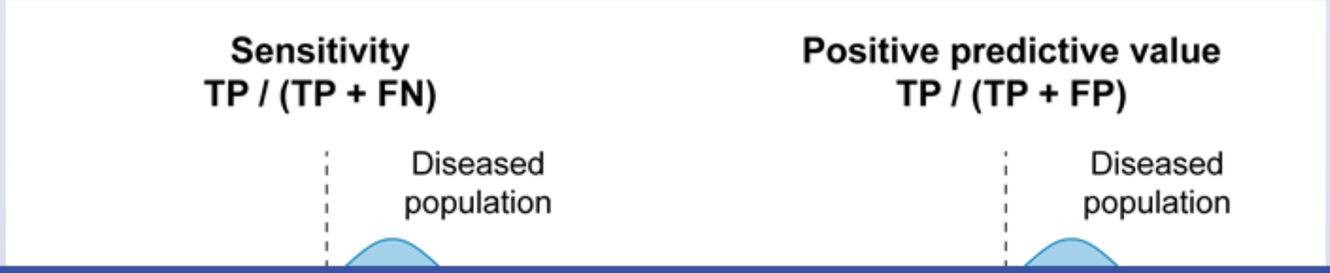
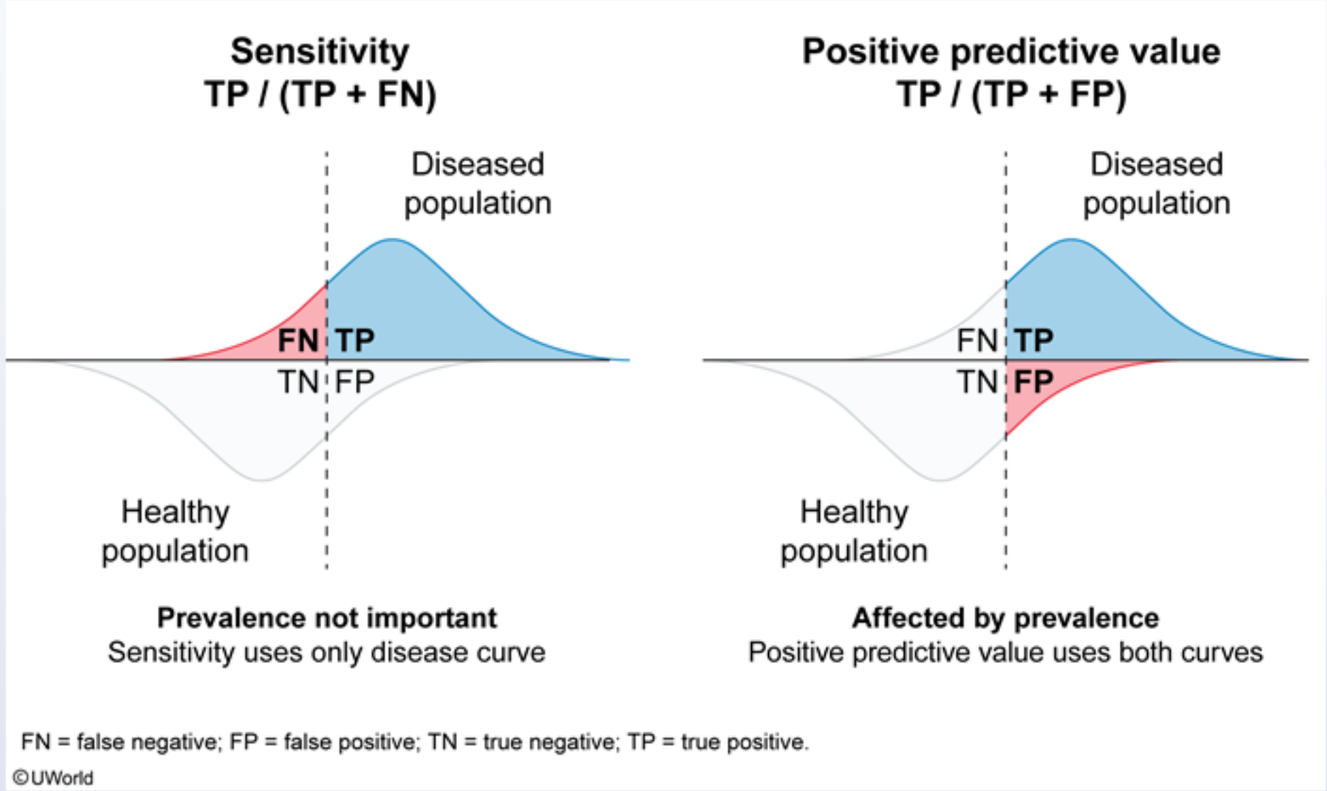
Explanation



Explanation



Predictive values are performance measures of diagnostic tests that are **dependent on the prevalence** of disease in a population of interest. The positive predictive value (**PPV**) is the probability that someone who tests positive actually has the disease. It is calculated by dividing the number of true-positive results by the total number of positive results (ie, **TP / [TP + FP]**). The number of true-positive results depends on the sensitivity, and the number of false-positive results depends on the specificity; the relative proportion of each is determined by the prevalence of disease in the population.

Populations with a lower disease prevalence have fewer true-positive results and higher numbers of false positives, so the PPV decreases. As

FN = false negative; FP = false positive; TN = true negative; TP = true positive.

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Populations with a lower disease prevalence have fewer true-positive results and higher numbers of false positives, so the PPV decreases. As disease prevalence increases, the number of true positives also increases, while the number of false positives decreases, resulting in a **higher PPV**. Similarly, the negative predictive value increases as the disease prevalence decreases.

(Choices A and B) Positive and negative likelihood ratios indicate how a particular positive or negative test result influences the pretest probability of having a disease. Likelihood ratios >1 indicate that the test result is associated with the presence of the disease; likelihood ratios <1 mean that the test result is associated with the absence of the disease. Because positive and negative likelihood ratios are based on sensitivity and specificity, they are not affected by disease prevalence.

(Choices D and E) Sensitivity and specificity are not affected by disease prevalence. This is because sensitivity is calculated using true positives and false negatives (only people with the disease), and specificity is calculated using true negatives and false positives (only people without the disease). In this case, the same test (with the same sensitivity and specificity characteristics) has been used on 2 different populations with a differing prevalence.

Educational objective:
Various parameters are used to evaluate the accuracy and usefulness of diagnostic tests. Positive and negative predictive values are influenced by disease prevalence in the target population; sensitivity, specificity, and likelihood ratios are not prevalence-dependent.

Biostatistics	Biostatistics & Epidemiology	Predictive values
Subject	System	Topic

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FN = false negative; FP = false positive; TN = true negative; TP = true positive.

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Predictive values are perf
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(Choices D and E) Sens
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Educational objective:
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Common performance measures for diagnostic tests

Parameter	Definition	Calculation
Sensitivity	The probability of a diseased person testing positive	Sensitivity = True positives / (True positives + False negatives)
Specificity	The probability of a nondiseased person testing negative	Specificity = True negatives / (True negatives + False positives)
Positive predictive value	The probability that disease is present given a positive result	PPV = True positives / (True positives + False positives)
Negative predictive value	The probability that disease is absent given a negative result	NPV = True negatives / (True negatives + False negatives)
Positive likelihood ratio	A ratio representing the likelihood of having the disease given a positive result	LR+ = Sensitivity / (1 − Specificity)
Negative likelihood ratio	A ratio representing the likelihood of having the disease given a negative result	LR− = (1 − Sensitivity) / Specificity

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FN = false negative; FP = false positive; TN = true negative; TP = true positive.

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	Positive condition	Negative condition	Total	
Positive test result	95 (**TP**)	18 (**FP**)	113	PPV = TP/(TP + FP)
Negative test result	5 (**FN**)	882 (**TN**)	887	NPV = TN/(TN + FN)
Total	100	900	1000	

Prevalence = 100/1000 = 0.10

Sensitivity = 95/(95 + 5) = 0.95
Specificity = 882/(18 + 882) = 0.98

PPV = 95/(95 + 18) = 0.84
NPV = 882/(5 + 882) = 0.99

PLR = 0.95/(1 − 0.98) = 47.5
NLR = (1 − 0.95)/0.98 = 0.05

	Positive condition	Negative condition	Total
Positive test result	380	12	392
Negative test result	20	588	608
Total	400	600	1000

Prevalence = 400/1000 = 0.40

Sensitivity = 380/(380 + 20) = 0.95
Specificity = 588/(12 + 588) = 0.98

PPV = 380/(380 + 12) = 0.97
NPV = 588/(20 + 588) = 0.97

PLR = 0.95/(1 − 0.98) = 47.5
NLR = (1 − 0.95)/0.98 = 0.05

FN = false negative; **FP** = false positive; **NLR** = negative likelihood ratio; **NPV** = negative predictive value; **PLR** = positive likelihood ratio; **PPV** = positive predictive value; **TN** = true negative; **TP** = true positive.

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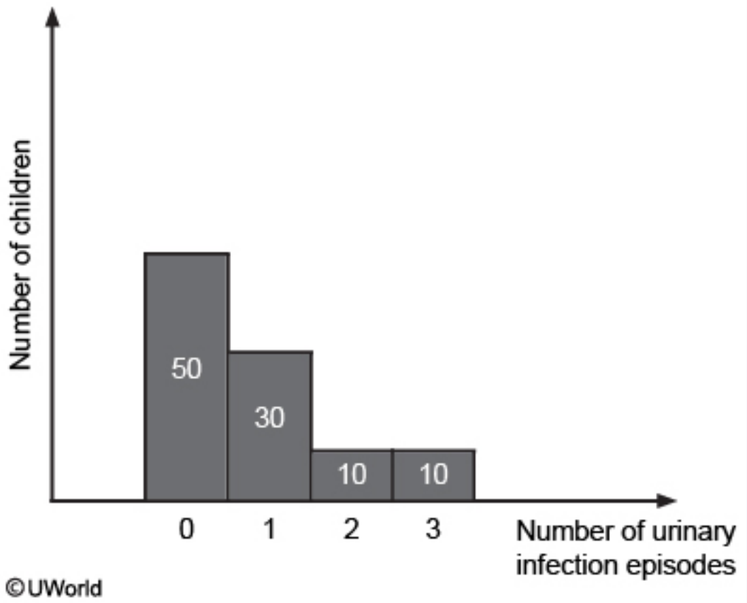
A sample of children age 2-5 years is chosen at random from an outpatient clinic. The number of urinary tract infections (UTIs) over a 1-year period is given in the figure below.



What was the average number of UTI episodes over 1 year for a child in this sample?

A. Between 0 and 1
B. 1
C. Between 1 and 2
D. 2
E. Between 2 and 3

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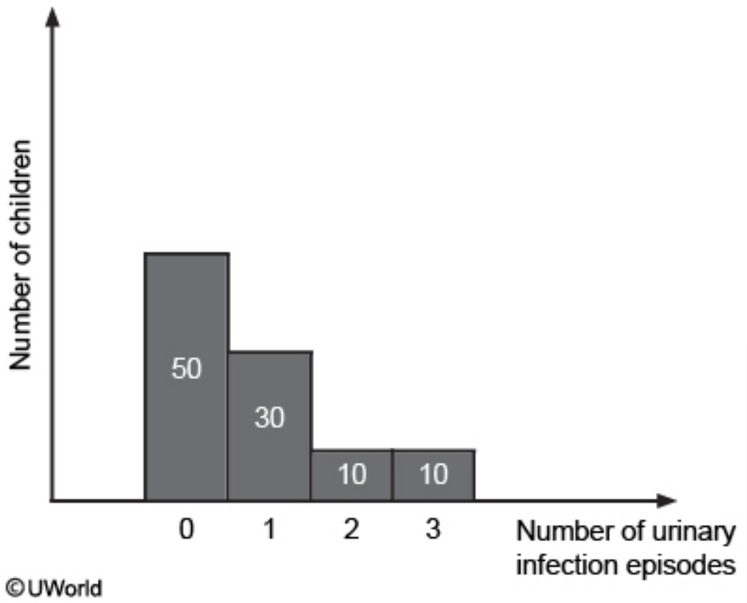
A sample of children age 2-5 years is chosen at random from an outpatient clinic. The number of urinary tract infections (UTIs) over a 1-year period is given in the figure below.



What was the average number of UTI episodes over 1 year for a child in this sample?

A. Between 0 and 1
B. 1
C. Between 1 and 2
D. 2
E. Between 2 and 3

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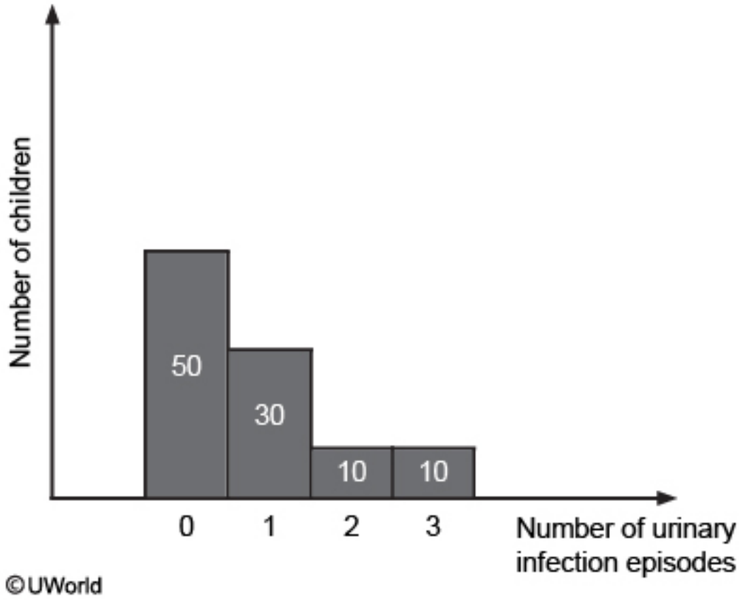

What was the average number of UTI episodes over 1 year for a child in this sample?

- A. Between 0 and 1 (75%)
- B. 1 (4%)
- C. Between 1 and 2 (16%)
- D. 2 (1%)
- E. Between 2 and 3 (2%)

Omitted
Correct answer

75%
Answered correctly

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D. 2 (1%)

E. Between 2 and 3 (2%)

Omitted
Correct answer
A

75%
Answered correctly

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Explanation

This bar graph illustrates the frequency of urinary tract infection (UTI) episodes in the sample. According to the figure, 50 children had 0 UTIs, 30 children had 1 UTI, 10 had 2 UTIs, and 10 had 3 UTIs.

In general, the average (or mean) of a dataset is the sum of the values divided by the total number of values. In this example, the average number of UTI episodes per child is the sum (ie, total number) of UTIs divided by the total sample size (ie, total number of children). The total sample size is: 50 + 30 + 10 + 10 = 100 children. The total number of UTIs is: (0 × 50) + (1 × 30) + (2 × 10) + (3 × 10) = 0 + 30 + 20 + 30 = 80 UTIs. The average is obtained by dividing the total number of UTIs (80) by the total sample size (100). Therefore, the average number of UTI episodes per year = 80/100 = 0.8 UTIs for a child in this sample.

In conclusion, children age 2-5 years in this clinic experienced between 0 and 1 UTI over 1 year on average.

Educational objective:
The average (or mean) of a dataset of values is the sum of the values divided by the total number of values.

Biostatistics	Biostatistics & Epidemiology	Urinary tract infection
Subject	System	Topic

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A 54-year-old man with hypertension and hyperlipidemia who came to the emergency department with chest pain wants to know if he is having a heart attack. Test A is newly available for diagnosing myocardial infarction (MI). In a recent study, the results of test A (compared to a gold standard diagnosis of MI) were as follows:

	MI	No MI
Test A positive	200	50
Test A negative	120	80

The patient has a positive result on test A. Assuming his pre-test probability is equivalent to the prevalence of MI in the study, what is the probability that the patient has an MI?

A. 40%
B. 50%
C. 60%
D. 80%
E. 90%

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- A. 40% (2%)
- B. 50% (1%)
- C. 60% (12%)
- ✓ D. 80% (82%)
- E. 90% (1%)

Omitted
Correct answer
D

82%
Answered correctly

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Explanation

Explanation

The **positive predictive value (PPV)** of a diagnostic test answers the following question: Given a positive test result, what is the probability that a patient has the disease? PPV corresponds to the number of people with the disease who test positive among all those who test positive. Using a standard contingency (2 × 2) table, PPV = a / (a + b).

Contingency table example: MI research study

Generic

	Disease positive	Disease negative	
Test positive	a True positive	b False positive	a+b
Test negative	c False negative	d True negative	c+d
	a+c	b+d	

Test A

	MI	No MI	
Test A Positive	200	50	250
Test A negative	120	80	200
	320	130	

MI = myocardial infarction.

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Unlike specificity and sensitivity, PPV varies with disease prevalence. If disease prevalence increases, PPV increases; similarly, PPV decreases with decreasing prevalence. In this question, the patient's pre-test probability (which takes into account clinical judgment regarding how likely it is that he has an MI) is assumed to be equivalent to the prevalence of MI in the study, making the results directly translatable. Therefore, PPV = 200 / (200+50) = 200/250 = 0.8 or 80%. In other instances, clinicians may assume that pre-test prevalence equals disease prevalence in the

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	Disease positive	Disease negative	
Test positive	a True positive	b False positive	a+b
Test negative	c False negative	d True negative	c+d
	a+c	b+d	

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Educational objective:
Positive predictive value represents the probability of truly having a disease given a positive test result. It increases with increasing disease prevalence and decreases with decreasing disease prevalence.

Biostatistics	Biostatistics & Epidemiology	Sensitivity, specificity, positive predictive value PPV, negative predictive value NPV
Subject	System	Topic

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A group of psychiatrists has noticed an unusual number of older individuals with depression in the surrounding community. A decision is taken to conduct a cross-sectional study to estimate the prevalence of depression in this specific population. Estimates for the prevalence of depression (cases per 100 individuals) in the community are as follows:

Age group	Women	Men
60-69	9.1	8.4
70-79	11.9	10.4
80-89	13.5	12.4
90+	13.3	12.1
Total	11.9	10.8

Suppose during an afternoon clinic, a psychiatrist sees a 65-year-old woman, a 72-year-old man, and an 84-year-old woman from this community. Assuming no relation between the 3 patients, what is the probability that none of them has depression?

A. 0.001
B. 0.011
C. 0.295
D. 0.705
E. 0.999

Submit

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Total	11.9	10.8

Suppose during an afternoon clinic, a psychiatrist sees a 65-year-old woman, a 72-year-old man, and an 84-year-old woman from this community. Assuming no relation between the 3 patients, what is the probability that none of them has depression?

A. 0.001 (8%)
B. 0.011 (6%)
C. 0.295 (8%)
D. 0.705 (66%)
E. 0.999 (10%)

Omitted
Correct answer
D

66%
Answered correctly

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Time Spent

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Last Updated

Explanation

Patient	Probability of having depression	Probability of *NOT* having depression
65-year-old woman	0.091	1 − 0.091
72-year-old man	0.104	1 − 0.104
84-year-old woman	0.135	1 − 0.135

The age- and gender-specific prevalence of depression in the community is a good estimator of the probability that a corresponding individual from community has the disease. Because each of the 3 patients is **unrelated** to the others, each of the diagnoses is an **independent event** (ie, a patient's diagnosis has no impact on another's). When events are independent of each other, the probability that all the events occur is calculated by **multiplying together** the probability of each individual event.

In this case, to calculate the probability that none of the 3 patients has depression, multiply the probability of each **complementary event** (ie, the probability of *not* having depression):

$$(1 - 0.091) \times (1 - 0.104) \times (1 - 0.135) = 0.909 \times 0.896 \times 0.865 = 0.705$$

(Choices A and E) The probability that all 3 patients have depression can be calculated by multiplying the probability of each event, (0.091) × (0.104) × (0.135) = 0.001. The complementary event (ie, the probability that at least 1 patient does not have depression) can be calculated by subtracting the probability that all 3 patients have depression from 1, or 1 − [(0.091) × (0.104) × (0.135)] = 0.999.

(Choice B) The probability that only the women have depression can be calculated by multiplying together the probability of each woman having the disorder along with the probability of the man *not* having the disorder, (0.091) × (0.135) × (1 − 0.104) = 0.011.

(Choice C) The probability that at least 1 patient has depression is complementary to the probability of none of the 3 patients having depression. It can be calculated by subtracting the probability that none of the 3 patients has depression from 1, or 1 − [(1 − 0.091) × (1 − 0.104) × (1 − 0.135)] = 0.295.

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Educational objective:
The multiplication law of probability states that the probability of 2 or more independent events occurring together can be calculated by multiplying the individual probabilities of each event. The multiplication law of probability can be extended to complementary events (1 − probability of event) in the same manner.

Biostatistics	Biostatistics & Epidemiology	Probability theory
Subject	System	Topic

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A novel serum biomarker, UWRLD99, is being evaluated for early detection of pancreatic cancer. The concentration of UWRLD99 (measured in international units [IU] per dL) has been found to be elevated in patients with pancreatic adenocarcinoma. Test results in 200 volunteers ("healthy") and 190 patients with biopsy-proven pancreatic cancer ("diseased") are given in the figure below. The investigators determined the sensitivity and specificity of UWRLD99 for pancreatic cancer using a cutoff of 200 IU/dL (indicated by the solid vertical line).

If they had instead used a lower cutoff as indicated by the dashed vertical line, which of the following would most likely be seen?

A. Higher number of false negatives

B. Higher positive predictive value

C. Higher sensitivity

D. Lower number of false positives

E. Lower number of true positives

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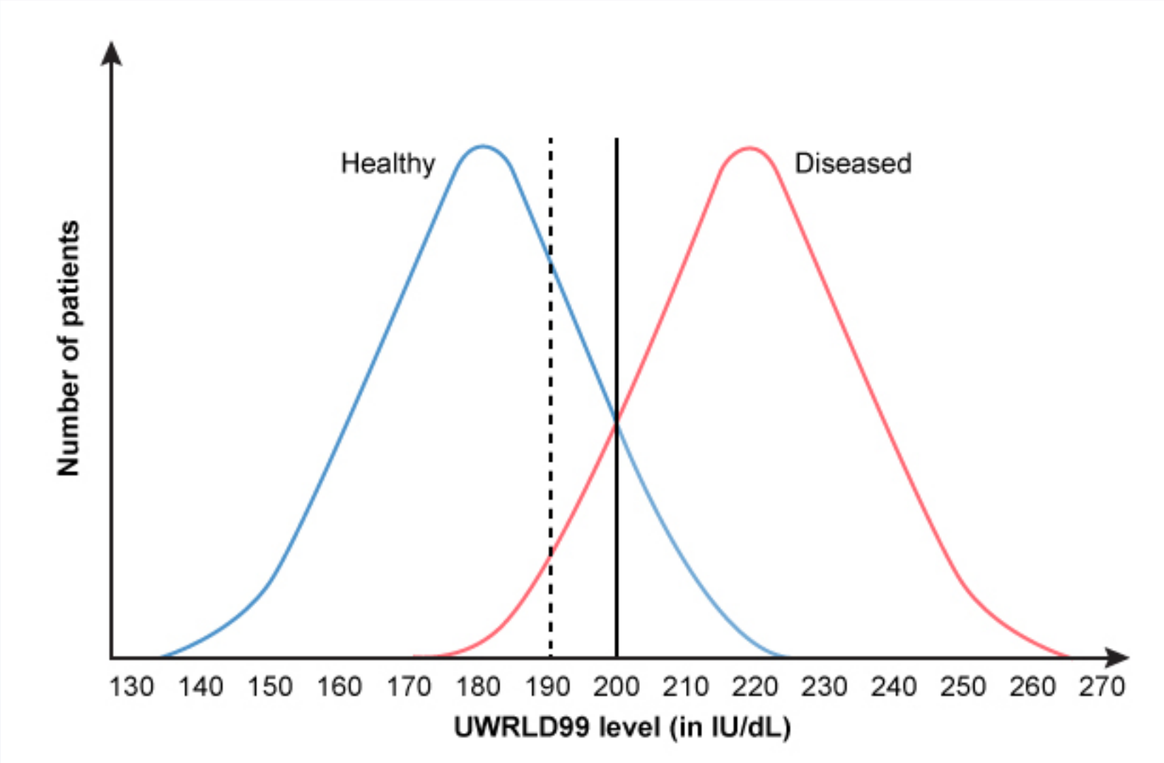
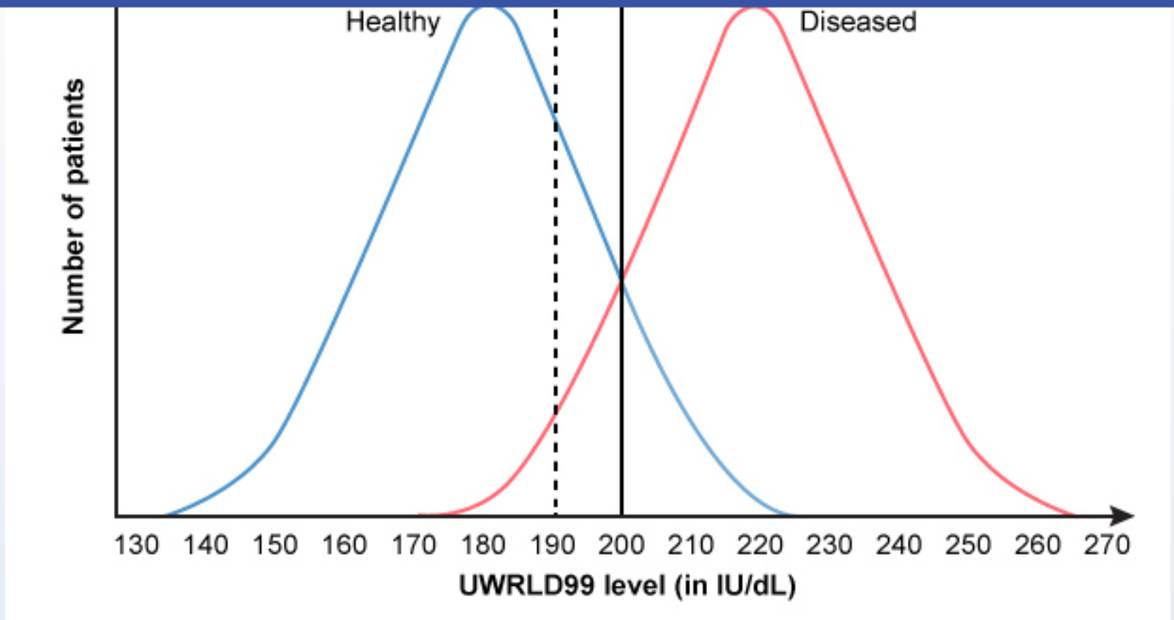


If they had instead used a lower cutoff as indicated by the dashed vertical line, which of the following would most likely be seen?

A. Higher number of false negatives

B. Higher positive predictive value



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- A. Higher number of false negatives
- B. Higher positive predictive value
- C. Higher sensitivity
- D. Lower number of false positives
- E. Lower number of true positives

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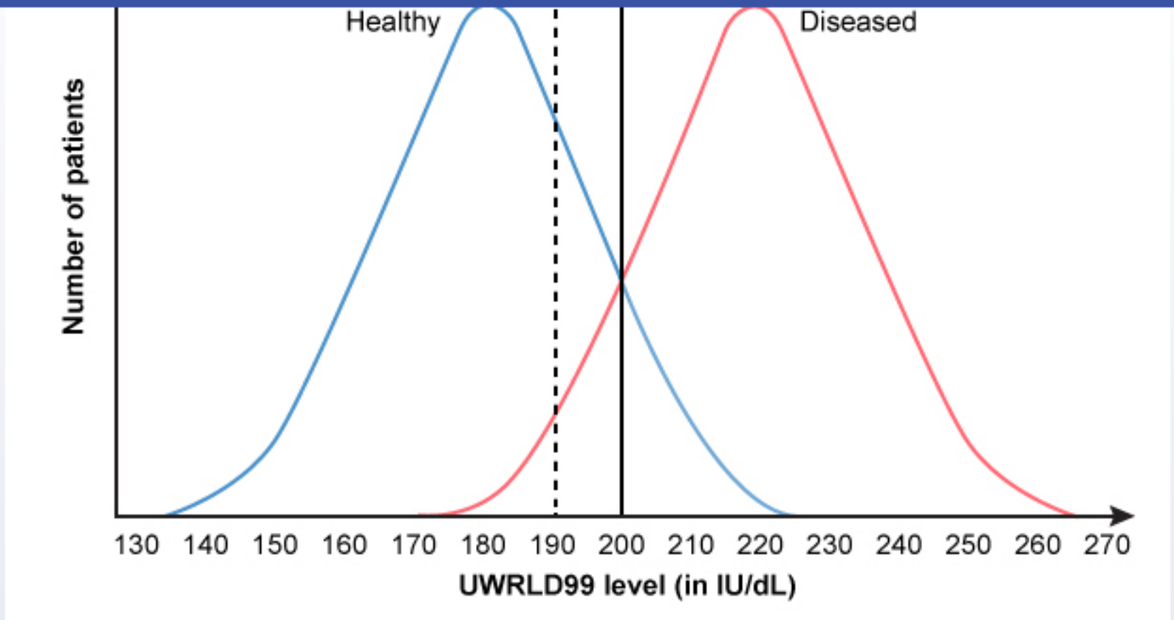

If they had instead used a lower cutoff as indicated by the dashed vertical line, which of the following would most likely be seen?

- A. Higher number of false negatives (8%)
- B. Higher positive predictive value (9%)
- ✓ C. Higher sensitivity (66%)
- D. Lower number of false positives (5%)
- E. Lower number of true positives (9%)

Omitted
Correct answer

66%
Answered correctly

10 secs
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02/14/2020
Last Updated

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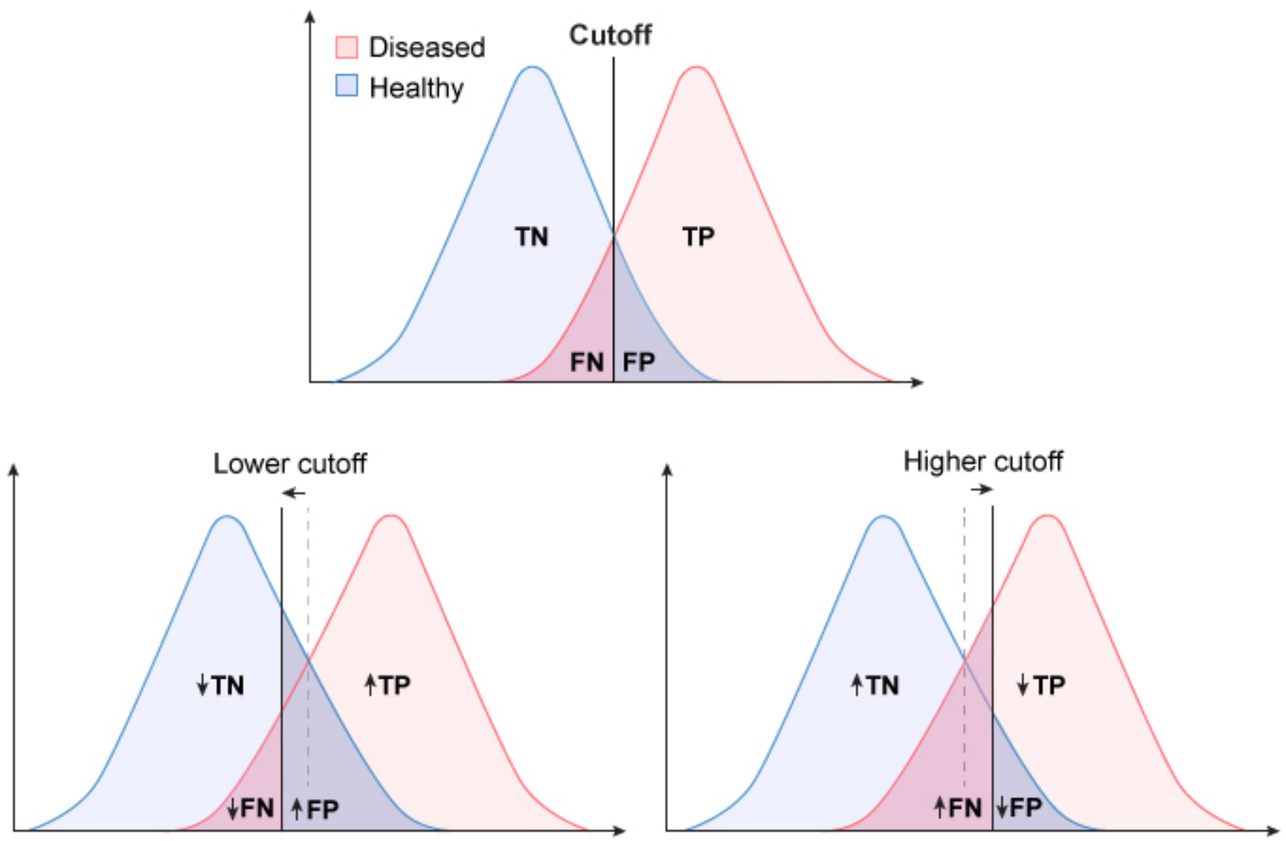

FN = false negatives; FP = false positives; TN = true negatives; TP = true positives

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Important parameters of diagnostic tests include the following:

- True positives (TP) represent diseased individuals with positive test results.
- True negatives (TN) represent healthy individuals with negative test results.
- False positives (FP) represent healthy individuals with positive test results.

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Important parameters of diagnostic tests include the following:

- True positives (TP) represent diseased individuals with positive test results.
- True negatives (TN) represent healthy individuals with negative test results.
- False positives (FP) represent healthy individuals with positive test results.
- False negatives (FN) represent diseased individuals with negative test results.
- **Sen**sitivity (TP/ [TP + FN]) represents a test's ability to correctly identify diseased individuals from among all individuals. A test with high sensitivity has a low FN rate (important for screening purposes). With a highly sensitive test, most diseased patients will have a positive test result (and a **n**egative test result would help rule **out** the disease [**SnNOut**]).
- **Sp**ecificity (TN/ [TN + FP]) represents the ability of a test to exclude those without the disease. A very specific test has a low FP rate (important for confirmatory tests). With a highly specific test, most healthy patients will have a negative test result (and a **p**ositive test result would help rule **in** the disease **[SpPIn]**).

The **cutoff value** of a quantitative diagnostic test determines whether a given result is interpreted as **positive or negative**. Depending on the disease or condition being tested for, sensitivity or specificity may be preferred and the cutoff value adjusted accordingly. A cutoff value just outside the overlapping region of the curves can maximize the sensitivity or specificity at 100% by correctly classifying all diseased or healthy individuals, respectively.

In the above example, changing the cutoff point to a **lower value** (shift to the left) would cause more patients with the disease to test positive (↑TP, ↓FN), **increasing the sensitivity** of the test. However, as a consequence, more patients without the disease would also test positive (↓TN, ↑FP), resulting in **decreased specificity**.

(Choices A, D, and E) Raising the cutoff value (shift to the right) would cause fewer individuals with the disease to have a positive test result (↓TP, ↑FN), so sensitivity would decrease. Fewer individuals without the disease would also test positive (↑TN, ↓FP), so specificity would increase.

(Choice B) Positive predictive value (PPV = TP / [TP + FP]) represents the probability that a patient with a positive test result actually has the disease. In this case, the lower cutoff value would increase both TP and FP; how this affects the PPV depends on **disease prevalence**, which is not provided. In a population with very low disease prevalence, the number of FP would be expected to increase proportionately more than the number of TP, which would lower the PPV.

(important for confirmatory tests). With a highly specific test, most healthy patients will have a negative test result (and a **p**ositive test result would help rule **in** the disease **[SpPIn]**).

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Educational objective:
The cutoff value of a quantitative diagnostic test determines whether a given result is interpreted as positive or negative. Lowering the cutoff point typically causes more patients with the disease to test positive, decreasing the number of false negatives and increasing test sensitivity. Consequently, more patients without the disease will also test positive, resulting in an increased number of false positives and decreased specificity.

Biostatistics	Biostatistics & Epidemiology	Quantitative diagnostic tests
Subject	System	Topic

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An 89-year-old man is brought to a geriatric clinic by family members who are concerned that he is developing dementia due to recent worsening of his memory. The attending physician uses a new cognitive test (test X) to help rule out the possibility of dementia. The patient's test result is negative. A study evaluating the efficacy of test X in a sample of 200 individuals age ≥85, in which the prevalence of dementia is 50%, has determined that the test has a specificity of 80% and a sensitivity of 90%. Assuming that this patient's pretest probability of having dementia is equivalent to the disease prevalence in the study population, what is the probability that this patient truly does not have dementia?

A. 18%

B. 53%

C. 66%

D. 82%

E. 89%

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D. 82%

E. 89%

Submit

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- A. 18% (4%)
- B. 53% (4%)
- C. 66% (8%)
- D. 82% (25%)
- ✓ E. 89% (56%)

Omitted
Correct answer
E

56%
Answered correctly

36 secs
Time Spent

05/08/2020
Last Updated

Explanation

The **negative predictive value** (NPV) of a diagnostic test is the probability that a patient truly **does not have the disease** when the patient receives a **negative test** result. It can be calculated from study data as follows:

NPV = number of true negatives / total number of negative tests

To determine the NPV in this case, it helps to summarize the results of the efficacy study in a 2 × 2 table. The study evaluated 200 individuals in a population with a 50% prevalence of dementia (ie, 100 patients had dementia while 100 did not). Knowing that specificity (ie, true negatives/total

The **negative predictive value** (NPV) of a diagnostic test is the probability that a patient truly **does not have the disease** when the patient receives a **negative test** result. It can be calculated from study data as follows:

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Standard 2 x 2 contingency table

	Disease present	Disease absent	
Test positive	a (true positive)	b (false positive)	a + b
Test negative	c (false negative)	d (true negative)	c + d
	a + c	b + d	

Test X

	Dementia present	Dementia absent	
Test X positive	90	20	110
Test X negative	10	80	90
	100	100	

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The NPV can now be estimated as follows:

NPV = number of true negatives (d) / total number of negative tests (c + d)

NPV = d / (c + d) = 80 / (10 + 80) = 0.889 = ~ **89%**

positive	(true positive)	(false positive)	
Test negative	c (false negative)	d (true negative)	c + d
	a + c	b + d	

positive			
Test X negative	10	80	90
	100	100	

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The NPV can now be estimated as follows:

NPV = number of true negatives (d) / total number of negative tests (c + d)

NPV = d / (c + d) = 80 / (10 + 80) = 0.889 = ~ **89%**

Unlike sensitivity and specificity, positive and negative predictive values vary based on the prevalence of the disease. In fact, the NPV is inversely proportional to the prevalence of a disease (eg, NPV ↓ as disease prevalence ↑). For the NPV to be applicable to an individual patient, that patient's **pretest probability** (eg, probability of having the disease before testing) must be **similar** to the **prevalence of disease** in the population where the study was conducted. The question says to assume that the patient's pretest probability is equivalent to the disease prevalence in the study population, so the NPV calculated in the study is generalizable to this patient.

Educational objective:
Negative predictive value (NPV) represents the probability of not having a disease given a negative test result. NPV is inversely proportional to the prevalence of a disease. When a patient has characteristics similar to the overall population (eg, age, sex, risk factor status), the disease prevalence is a valid estimate of the pretest probability of disease.

Biostatistics	Biostatistics & Epidemiology	Predictive values
Subject	System	Topic

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A physician research group is evaluating the efficacy of a new lipid-lowering drug, Superstatin, which is being marketed directly to consumers as a groundbreaking new therapy to prevent heart attacks. The drug manufacturer claims that the drug is more effective than existing hypolipidemic agents for primary prevention of myocardial infarction. Results of a 5-year, randomized, double-blinded, controlled study to evaluate the efficacy of Superstatin are shown below.

	Number of patients treated with Superstatin	Number of patients treated with control medication
Myocardial infarction	10	25
No myocardial infarction	990	975

Compared to the control medication, how many patients need to be treated with Superstatin to prevent one additional myocardial infarction?

A. 2
B. 5
C. 23
D. 48
E. 67
F. 92
G. 100

Submit

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

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	Number of patients treated with Superstatin	Number of patients treated with control medication
Myocardial infarction	10	25
No myocardial infarction	990	975

Compared to the control medication, how many patients need to be treated with Superstatin to prevent one additional myocardial infarction?

A. 2 (7%)
B. 5 (11%)
C. 23 (5%)
D. 48 (4%)
✓ E. 67 (60%)
F. 92 (2%)
G. 100 (7%)

Omitted
Correct answer
E

60%
Answered correctly

02 secs
Time Spent

05/01/2020
Last Updated

Common measures of therapeutic efficacy		
Term	**Definition**	**Calculation**
Absolute risk reduction (ARR)	Percentage indicating the actual difference in event rate between control & treatment groups	ARR = control rate – treatment rate
Relative risk reduction (RRR)	Percentage indicating relative reduction in the treatment event rate compared to the control group	RRR = ARR/control rate
Relative risk (RR)	Ratio of the probability of an event occurring in the treatment group compared to the control group	RR = treatment rate/control rate
Number needed to treat (NNT)	Number of individuals that need to be treated to prevent a negative outcome in 1 patient	NNT = 1/ARR

The **number needed to treat (NNT)** represents the number of patients that need to be treated with a medication (eg, Superstatin) in order to **prevent** an additional **negative outcome** (eg, myocardial infarction). NNT is calculated by dividing 1 by the **absolute risk reduction** (ARR).

NNT = 1 / ARR

ARR represents the actual difference in control and experimental group event rates. The data is *not* presented in the standard format of a contingency (2 × 2) table, so care should be exercised in selecting the appropriate values. In this example, the event of interest is myocardial infarction. There were 25 + 975 = 1,000 patients in the control group; of those, 25 had a myocardial infarction. Similarly, there were 10 + 990 = 1,000 patients in the treatment (ie, Superstatin) group; of those, 10 had a myocardial infarction. Therefore:

Control event rate = 25 / 1,000 = 0.025

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Control event rate = 25 / 1,000 = 0.025

Experimental event rate = 10 / 1,000 = 0.01

ARR can then be calculated:

ARR = Control event rate – Experimental event rate = 0.025 – 0.01 = 0.015, or 1.5%

Finally, NNT is found by dividing 1 by 0.015:

NNT = 1 / 0.015 = 66.6 ≈ 67

Rounding up the result to the nearest whole number, **67 patients** need to be treated with Superstatin to prevent an additional myocardial infarction.

The ideal NNT would be 1, meaning that all patients in the treatment group benefit from the treatment. A **low NNT** implies that a treatment is **more beneficial** because fewer patients need to be treated to prevent an additional negative outcome. For instance, if a third hypolipidemic medication had an NNT of 40, it would be more beneficial than Superstatin, as only 40 patients would need to be treated over a given period to prevent an additional myocardial infarction.

Educational objective:
The number needed to treat (NNT) is the number of patients that need to be treated with a medication to avoid an additional negative outcome. NNT is calculated by dividing 1 by the absolute risk reduction (the difference between the control and experimental group event rates). Lower NNT values represent more beneficial treatments.

Biostatistics	Biostatistics & Epidemiology	Number Needed To Treat
Subject	System	Topic

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Biostatistics	Biostatistics & Epidemiology	Number Needed To Treat
Subject	System	Topic

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The **number needed to treat (NNT)** represents the number of patients that need to be treated with a medication (eg, Superstatin) in order to **prevent** an additional **negative outcome** (eg, myocardial infarction). NNT is calculated by dividing 1 by the **absolute risk reduction** (ARR).

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Educational objective:
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Exhibit Display

	Outcome/disease present	Outcome/disease absent	
Exposure/risk factor present	a	b	a + b
Exposure/risk factor absent	c	d	c + d
	a + c	b + d	

Add To New Card | Existing Card

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A study is performed to compare the effect of tramadol when compared to placebo for painful polyneuropathy. Fifty patients are selected and randomly allocated to 1 of 2 treatment sequences: Tramadol followed by placebo, or placebo followed by tramadol. The initial treatment period is delivered for 4 weeks followed by an interim 1-week washout phase, after which the second treatment period is delivered for an additional 4 weeks. After each treatment period, patients use a 10-point numeric scale to rate pain, paresthesia, and tenderness. Which of the following best describes this study design?

A. Case-control study
B. Case series study
C. Crossover study
D. Cross-sectional study
E. Prospective cohort study
F. Retrospective cohort study

Submit

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- A. Case-control study (11%)
- B. Case series study (5%)
- ✓ C. Crossover study (64%)
- D. Cross-sectional study (3%)
- E. Prospective cohort study (12%)
- F. Retrospective cohort study (1%)

Omitted
Correct answer
C

64%
Answered correctly

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04/25/2020
Last Updated

Explanation

Crossover study design

Wash out period

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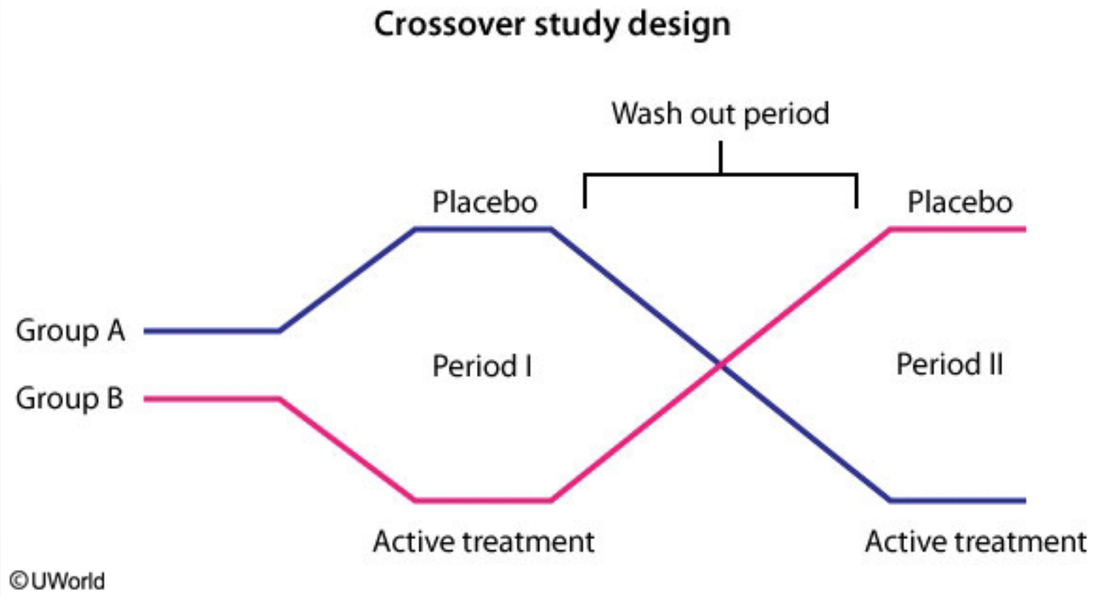

In this example, patients are allocated to 1 of 2 treatment groups: Group A receives placebo followed by tramadol and Group B receives tramadol followed by placebo. After the initial 4-week treatment period and the 1-week washout phase, the **treatments are switched** and delivered for an additional 4 weeks. This is consistent with a **crossover study**, in which subjects are randomly allocated to a sequence of 2 or more treatments given consecutively. The simplest model is the AB/BA type of study in which half of the subjects are allocated to the AB study arm and receive treatment A followed by treatment B, while the other half of the subjects are allocated to the BA study arm and receive the same treatments but in reverse order. In this way, crossover trials allow the patients to serve as their **own controls**.

The principal drawback of crossover trials is that the effects of one treatment may **carry over** and alter the response to a subsequent treatment. To avoid this, a **washout phase** (no treatment) is often added between treatments. The washout period is designed to be long enough to allow the effects of prior treatment to wear off.

(Choice A) A case-control study is designed by selecting patients with a particular disease (cases) and without that disease (controls), then determining their past exposure status to ≥1 risk factors believed to be associated with the disease of interest.

(Choice B) A case series is a descriptive study that tracks patients with a known condition (eg, a particular exposure, risk factor, or disease) to

additional 4 weeks. This is consistent with a **crossover study**, in which subjects are randomly allocated to a sequence of 2 or more treatments given consecutively. The simplest model is the AB/BA type of study in which half of the subjects are allocated to the AB study arm and receive treatment A followed by treatment B, while the other half of the subjects are allocated to the BA study arm and receive the same treatments but in reverse order. In this way, crossover trials allow the patients to serve as their **own controls**.

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(Choice B) A case series is a descriptive study that tracks patients with a known condition (eg, a particular exposure, risk factor, or disease) to document the natural history or response to treatment. Unlike a case-control study, a case series is a descriptive study that cannot quantify statistical significance.

(Choice D) A cross-sectional study is also known as a prevalence study. It is characterized by the simultaneous measurement of exposure and outcome. It is a snapshot study design that frequently uses surveys. These studies are relatively inexpensive and easy to perform.

(Choices E and F) Prospective cohort studies identify 2 groups of individuals (ie, cohorts), based on their exposure status to a risk factor. These 2 cohorts are then followed over time to assess development of the disease of interest. Sometimes the exposure status is determined retrospectively, typically using medical records, and patients are tracked from the point of exposure onward.

Educational objective:
In a crossover study, subjects are randomly allocated to a sequence of 2 or more treatments given consecutively. A washout (no treatment) period is often added between treatment intervals to limit the confounding effects of prior treatment.

Biostatistics	Biostatistics & Epidemiology	Study designs
Subject	System	Topic

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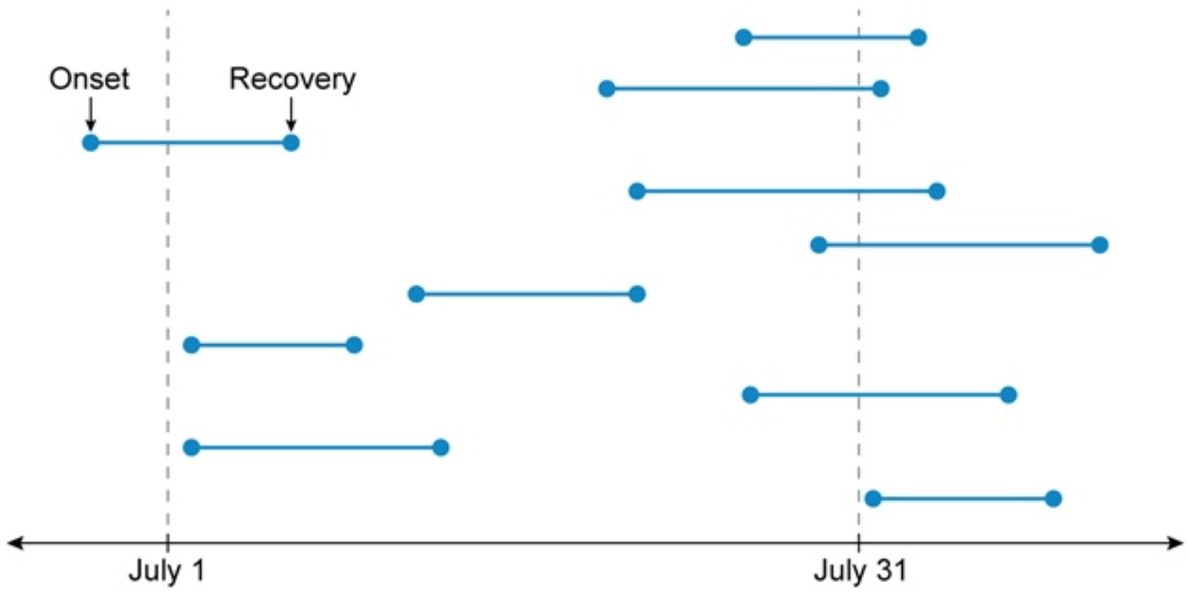
A study is conducted to estimate the prevalence of catheter-associated urinary tract infection (CAUTI) in the intensive care unit (ICU) of an urban hospital. The plot below shows the number of cases of CAUTI in this hospital during the month of July among patients in the ICU. Based on the plot, which of the following is the number of prevalent cases on July 31?



CAUTI = catheter-associated urinary tract infection; **ICU** = intensive care unit.

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A. 1

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C. 5

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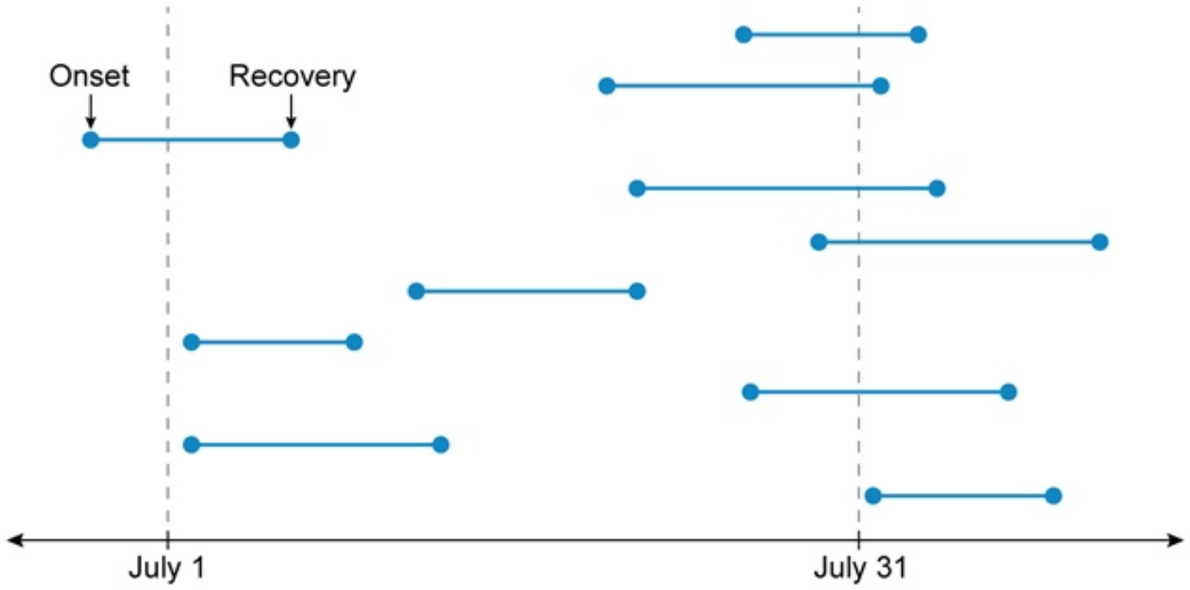

CAUTI = catheter-associated urinary tract infection; **ICU** = intensive care unit.

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D. 8
E. 9

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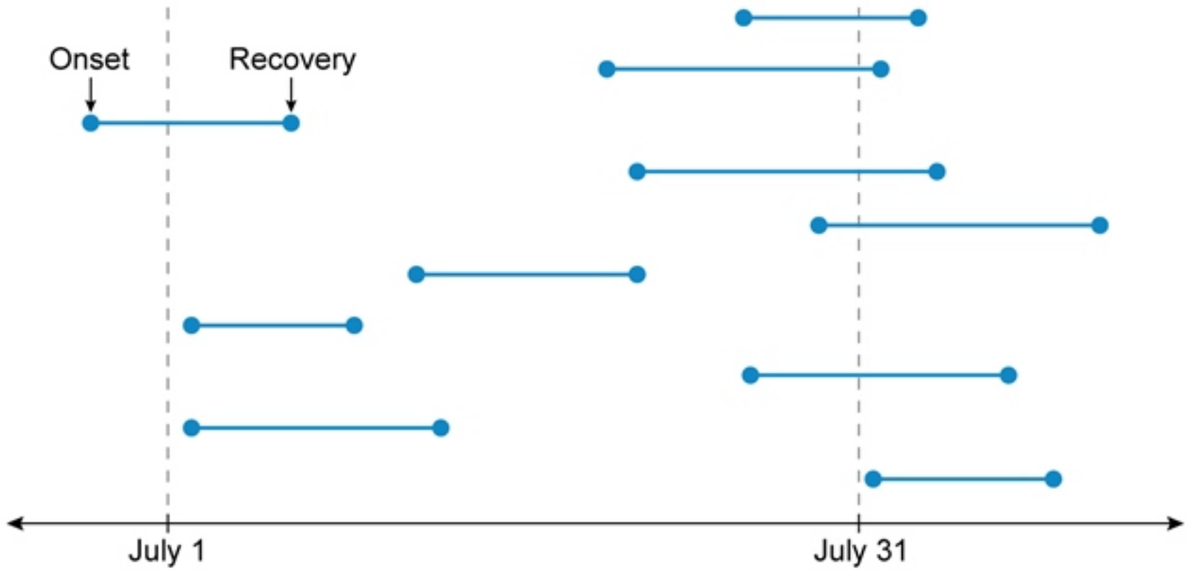

CAUTI = catheter-associated urinary tract infection; **ICU** = intensive care unit.

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A. 1 (1%)
B. 4 (0%)
✓ C. 5 (88%)
D. 8 (2%)
E. 9 (5%)

Omitted
Correct answer

88%
Answered correctly

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Time Spent

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Correct answer
C

Answered correctly

Time Spent

Last Updated

Explanation

Prevalence refers to the **proportion of diseased individuals** in a particular at-risk population, often measured in the following ways:

- **Period prevalence** refers to the number of disease cases in a period (eg, from July 1 to July 31) divided by the number of people in the at-risk population (ie, **prevalent cases** at the beginning of a period plus any **incident cases** during the period).
- **Point prevalence** refers to the number of **disease cases** that are active at a **specific point** in time (eg, July 31) divided by the number of people in the at-risk population.

In this example, a study determined the number of cases of catheter-associated urinary tract infection (CAUTI) among patients in the intensive care unit during the month of July. There were 9 cases of CAUTI in July; a tenth case developed after July 31. Four of the 9 patients recovered before July 31; therefore, the number of cases of CAUTI still active on July 31 was 5.

(Choice A) Only 1 patient had developed CAUTI before July 1; this represents the number of point-prevalent cases on July 1.

(Choice B) Four patients with CAUTI recovered during the month of July.

(Choice D) Eight cases of CAUTI developed between July 1 and July 31; this represents the number of incident cases during July.

(Choice E) There were 9 cases of CAUTI during the month of July; this represents the number of period-prevalent cases.

Educational objective:
Unlike period prevalence, point prevalence considers only the number of disease cases that are active at a specific point in time.

Biostatistics	Biostatistics & Epidemiology	Prevalence and incidence
Subject	System	Topic

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A state's population for 2016 was estimated at 4,000,000. At the beginning of the same year, the state reported having 20,000 cases of a rare and fatal neurodegenerative condition. At the end of 2016, the state reported 7,000 new cases, as well as 1,000 deaths attributable to this condition. Another 40,000 deaths from all other causes were also reported at the end of the year. What was the cumulative incidence of the disease in 2016?

A. 1,000 / 4,000,000
B. 6,000 / 3,980,000
C. 6,000 / 4,000,000
D. 7,000 / 3,980,000
E. 7,000 / 4,000,000
F. 26,000 / 3,959,000
G. 41,000 / 4,000,000

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A state's population for 2016 was estimated at 4,000,000. At the beginning of the same year, the state reported having 20,000 cases of a rare and fatal neurodegenerative condition. At the end of 2016, the state reported 7,000 new cases, as well as 1,000 deaths attributable to this condition. Another 40,000 deaths from all other causes were also reported at the end of the year. What was the cumulative incidence of the disease in 2016?

- A. 1,000 / 4,000,000 (0%)
- B. 6,000 / 3,980,000 (2%)
- C. 6,000 / 4,000,000 (1%)
- ✓ D. 7,000 / 3,980,000 (52%)
- E. 7,000 / 4,000,000 (30%)
- F. 26,000 / 3,959,000 (12%)
- G. 41,000 / 4,000,000 (0%)

Omitted
Correct answer
D

52%
Answered correctly

02 secs
Time Spent

05/09/2020
Last Updated

Explanation

Cumulative incidence (CI) is calculated as the total number of **new cases** of a disease (eg, neurodegenerative condition) over a **specific period** (eg, during 2016) divided by the number of **people at risk** at the **beginning** of the period. It does not account for deaths in the period under study because the patients who died were, at some point in the intervening period, still considered part of the baseline population at risk for the disease.

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Cumulative incidence (CI) is calculated as the total number of **new cases** of a disease (eg, neurodegenerative condition) over a **specific period** (eg, during 2016) divided by the number of **people at risk** at the **beginning** of the period. It does not account for deaths in the period under study because the patients who died were, at some point in the intervening period, still considered part of the baseline population at risk for the disease. In this case, there were 3,980,000 people at risk (ie, 4,000,000 − 20,000 already with the disease) at the beginning of 2016, and 7,000 new cases of the disease occurred over the 1-year period being analyzed. Therefore, the CI is:

CI = 7,000 / (4,000,000 − 20,000) = **7,000 / 3,980,000**

Unlike incidence rate (which is typically reported as the number of cases per person-year), CI does not incorporate time into the denominator; it is simply the proportion of at-risk individuals who contract the disease over the specified period.

(Choice A) The disease-specific mortality (in this example: 1,000 / 4,000,000) is the number of deaths attributable to a disease per year divided by the total population.

(Choice B) The CI does not account for deaths in the period under study. In this case, the numerator is 7,000, not 6,000.

(Choice C) The rate of increase of a disease (ie, the increase in disease prevalence) is the number of new cases per year minus the number of deaths (or cures) attributable to the disease per year, divided by the total population. This yields (7,000 − 1,000) / 4,000,000.

(Choice E) The CI is calculated by taking into consideration the population at risk at the beginning of the period under study. In this case, the denominator must be reduced by the number of cases reported at the beginning of the year 2016 (ie, 4,000,000 − 20,000 = 3,980,000).

(Choice F) The prevalence of disease at the end of 2016 takes into consideration the prevalent cases at the beginning of the year, the incident cases throughout the year, and all the deaths reported by the end of the year. In this case, the prevalence at the closing of 2016 is: ([20,000 + 7,000] – 1,000) / (4,000,000 – [40,000 + 1,000]).

(Choice G) The mortality rate is the number of deaths per year divided by the total population. This yields 41,000 / 4,000,000.

Educational objective:
The cumulative incidence of a disease is the number of new cases of a disease over a specific period divided by the total population at risk at the beginning of the study (ie, the proportion of at-risk individuals who contract the disease over the specified period).

Biostatistics Biostatistics & Epidemiology Prevalence and incidence

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Unlike incidence rate (which is typically reported as the number of cases per person-year), CI does not incorporate time into the denominator; it is simply the proportion of at-risk individuals who contract the disease over the specified period.

(Choice A) The disease-specific mortality (in this example: 1,000 / 4,000,000) is the number of deaths attributable to a disease per year divided by the total population.

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Educational objective:
The cumulative incidence of a disease is the number of new cases of a disease over a specific period divided by the total population at risk at the beginning of the study (ie, the proportion of at-risk individuals who contract the disease over the specified period).

Biostatistics	Biostatistics & Epidemiology	Prevalence and incidence
Subject	System	Topic

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Zeracizumab is an experimental angiogenesis inhibitor targeting vascular endothelial growth factor that is being tested for the treatment of advanced, chemotherapy-naive, non-squamous non-small cell lung cancer (NSCLC). Part of the drug company's evaluation process is to analyze the 1-year survival after treatment to determine the clinical efficacy of the experimental treatment. The results are given in the table below.

	Zeracizumab-containing regimen	Standard chemotherapy
Alive at 1 year	40	51
Dead at 1 year	60	69

Which of the following best represents the number needed to harm for the zeracizumab-containing regimen?

A. 2
B. 25
C. 40
D. 72
E. 94

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	Zeracizumab-containing regimen	Standard chemotherapy
Alive at 1 year	40	51
Dead at 1 year	60	69

Which of the following best represents the number needed to harm for the zeracizumab-containing regimen?

A. 2 (14%)
B. 25 (16%)
✓ C. 40 (59%)
D. 72 (6%)
E. 94 (3%)

Omitted
Correct answer
C

59%
Answered correctly

03 secs
Time Spent

05/07/2020
Last Updated

Explanation

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Unfortunately, not all interventions or new treatments end up helping patients. The **number needed to harm (NNH)** represents the number of people who must be treated before 1 additional adverse event occurs. It is calculated in a manner similar to the number needed to treat (NNT) but using the **absolute risk increase** (attributable risk) instead of the absolute risk reduction:

NNH = 1 / Absolute risk increase

To determine the absolute risk increase, first **calculate the adverse event rate** (eg, death) in the experimental and control groups. In this case, the adverse event of interest is death at 1 year. There were 40 + 60 = 100 people treated with the experimental treatment (ie, zeracizumab-containing regimen); of those, 60 were dead at 1 year. Similarly, there were 51 + 69 = 120 people treated with standard chemotherapy; of those, 69 were dead at 1 year. Therefore:

Adverse event rate in experimental group = 60 / 100 = 0.60 (ie, 60%)
Adverse event rate in control group = 69 / 120 = 0.575 (ie, 57.5%)

The absolute risk increase can then be calculated by **subtracting** the adverse event rate in the control group from the adverse event rate in the treatment group:

Absolute risk increase = 0.60 – 0.575 = 0.025 (ie, 2.5%)

The absolute risk increase attributable to the treatment is **2.5%** (60% risk of being dead at 1 year in the treatment group compared to 57.5% in the control group). The NNH then is simply the **inverse** of the absolute risk increase:

NNH = 1 / 0.025 = 40

This result indicates that, on average, **40 patients need to be treated** with a zeracizumab-containing regimen for 1 additional person to experience an adverse event (ie, death in 1 year).

Note that the data is NOT presented in the standard format of a contingency (2 × 2) table, so care should be exercised in selecting the appropriate values and applying the formulas (see alternate solution).

Educational objective:
The number needed to harm (NNH) represents the number of people who must be treated before 1 additional adverse event occurs. In order to calculate NNH, the absolute risk increase between the treatment and control groups must be known: NNH = 1 / Absolute risk increase

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Note that the data is NOT presented in the standard format of a contingency (2 × 2) table, so care should be exercised in selecting the appropriate values and applying the formulas (see alternate solution).

Educational objective:
The number needed to harm (NNH) represents the number of people who must be treated before 1 additional adverse event occurs. In order to calculate NNH, the absolute risk increase between the treatment and control groups must be known: NNH = 1 / Absolute risk increase

Biostatistics	Biostatistics & Epidemiology	Number Needed To Treat
Subject	System	Topic

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The absolute risk increase e treatment group:

The absolute risk increase the control group). The NNH

This result indicates that, experience an adverse ev

Note that the data is NOT iate values and applying the fo

Educational objective:
The number needed to ha to calculate NNH, the absolu

Biostatistics Subject | Biosta System

Exhibit Display

Number needed to harm (NNH)

Reordering the data into a standard contingency table format with the exposure of interest (ie, zeracizumab-containing regimen) in the second row and the outcome of interest (dead at 1 year) in the second column allows use of the standard formula for absolute risk increase:

$$[\, a / (a + b) \,] - [\, c / (c + d) \,]$$

	Dead at 1 year	Alive at 1 year
Zeracizumab-containing regimen	a = 60	b = 40
Standard chemotherapy	c = 69	d = 51

In this case: [a / (a + b)] – [c / (c + d)] = [60 / (60 + 40)] – [69 / (69 + 51)] = 60/100 – 69/120 = 0.60 – 0.575 = 0.025; so NNH = 1 / 0.025 = 40.

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A large cohort study is conducted to assess the association between smoking and squamous cell carcinoma of the esophagus among middle-aged Chinese men. During 10 years of follow-up, smokers have 5 times the risk of esophageal carcinoma compared to non-smokers (relative risk = 5.0, 95% confidence interval = 2.9-7.1). According to the study results, what percentage of squamous cell carcinoma of the esophagus in smokers can be attributed to smoking?

A. 25%

B. 50%

C. 70%

D. 80%

E. 90%

Submit

A large cohort study is conducted to assess the association between smoking and squamous cell carcinoma of the esophagus among middle-aged Chinese men. During 10 years of follow-up, smokers have 5 times the risk of esophageal carcinoma compared to non-smokers (relative risk = 5.0, 95% confidence interval = 2.9-7.1). According to the study results, what percentage of squamous cell carcinoma of the esophagus in smokers can be attributed to smoking?

A. 25% (12%)
B. 50% (13%)
C. 70% (10%)
✓ D. 80% (52%)
E. 90% (11%)

Omitted
Correct answer
D

52%
Answered correctly

02 secs
Time Spent

01/24/2020
Last Updated

Explanation

The **attributable risk percent in the exposed ($ARP_{exposed}$)** is an important measure of the impact of a risk factor. $ARP_{exposed}$ represents the excess risk in an exposed population that can be explained by exposure to a particular risk factor. It is calculated using the following formula:

$$ARP_{exposed} = 100 \times [(\text{risk in exposed} - \text{risk in unexposed})/\text{risk in exposed}]$$

This basic definition can be used to derive an equivalent formula involving relative risk (RR):

$ARP_{exposed} = 100 \times [(RR - 1)/RR]$, where RR = risk in exposed/risk in unexposed

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Correct answer
D

52%
Answered correctly

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Time Spent

01/24/2020
Last Updated

Explanation

The **attributable risk percent in the exposed ($ARP_{exposed}$)** is an important measure of the impact of a risk factor. $ARP_{exposed}$ represents the excess risk in an exposed population that can be explained by exposure to a particular risk factor. It is calculated using the following formula:

$ARP_{exposed}$ = 100 × [(risk in exposed – risk in unexposed)/risk in exposed]

This basic definition can be used to derive an equivalent formula involving relative risk (RR):

$ARP_{exposed}$ = 100 × [(RR – 1)/RR], where RR = risk in exposed/risk in unexposed

Applying the formula to this example:

$ARP_{exposed}$ = 100 × [(RR – 1)/RR] = 100 × [(5 – 1)/5] = 100 × (4/5) = 100 × 0.8 = 80%

Therefore, according to the study results, 80% of esophageal squamous cell carcinoma cases in smokers were attributable to smoking.

The $ARP_{exposed}$ is related to the attributable risk (AR), which is simply the difference between risk in the exposed and risk in the unexposed.

Educational objective:
The attributable risk percent (ARP) in the exposed represents the excess risk in the exposed population that can be attributed to the risk factor. It can be easily derived from the relative risk (RR) using the formula: $ARP_{exposed}$ = 100 × [(RR – 1)/RR].

Biostatistics	Biostatistics & Epidemiology	Risk
Subject	System	Topic

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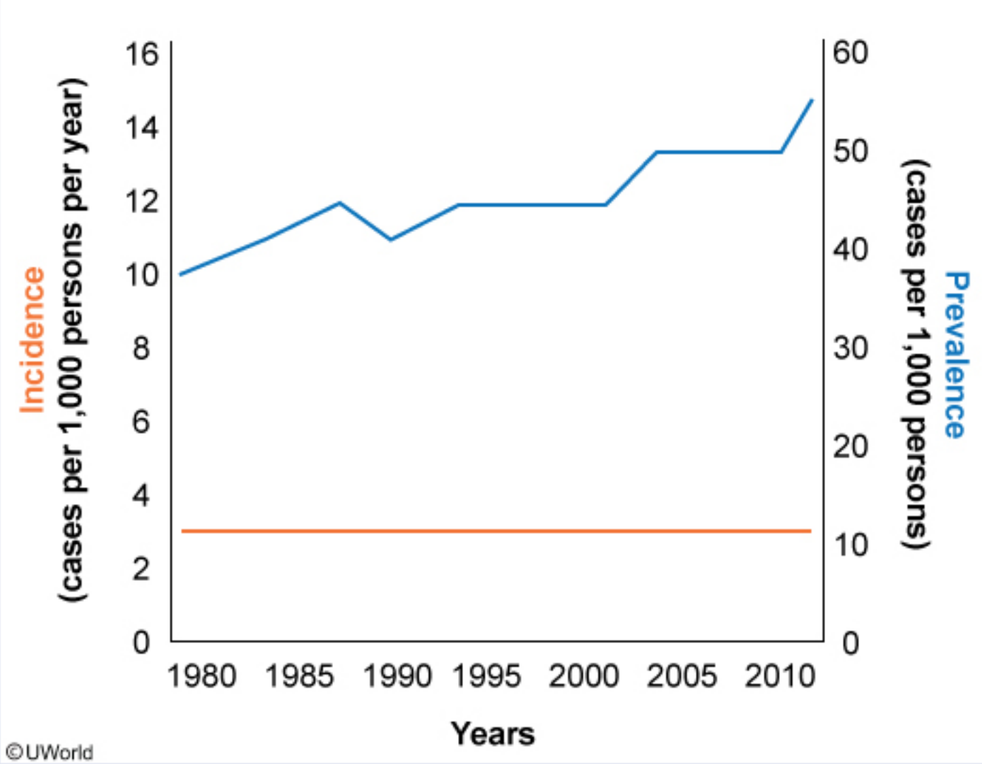
An epidemiological study is initiated to assess the impact of type II diabetes mellitus in a large population with little migration. Disease incidence and prevalence are monitored and recorded as the number of cases per 1,000 individuals over a 30-year period.



Which of the following is the most likely explanation for the change in disease prevalence seen in the graph?

A. Decreased hospitalization rate

B. High mortality in diabetics

C. Improved quality of care

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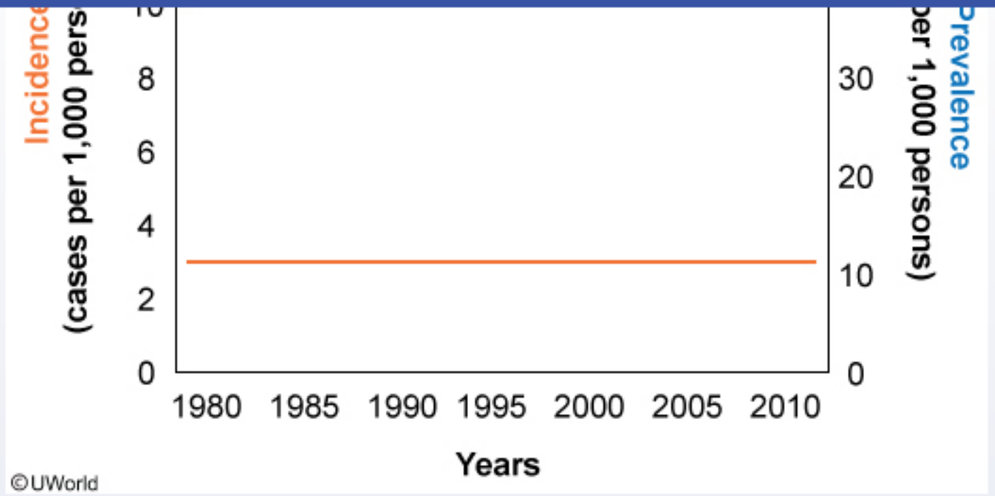

Which of the following is the most likely explanation for the change in disease prevalence seen in the graph?

- A. Decreased hospitalization rate
- B. High mortality in diabetics
- C. Improved quality of care
- D. Increased accuracy of diagnostic testing
- E. Increased exposure to risk factors
- F. Increased number of new diabetes cases
- G. Selective survival bias

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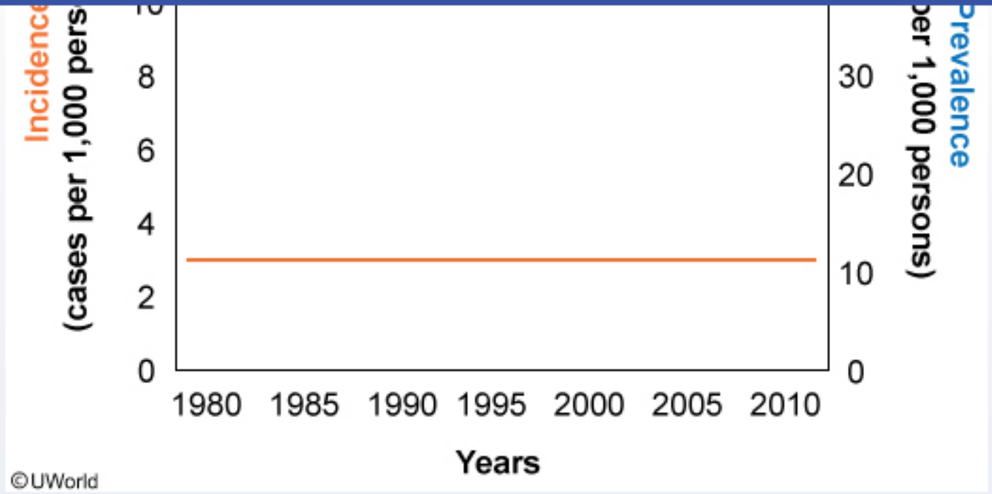

Which of the following is the most likely explanation for the change in disease prevalence seen in the graph?

- A. Decreased hospitalization rate (0%)
- B. High mortality in diabetics (1%)
- ✓ C. Improved quality of care (76%)
- D. Increased accuracy of diagnostic testing (7%)
- E. Increased exposure to risk factors (3%)
- F. Increased number of new diabetes cases (5%)
- G. Selective survival bias (3%)

Omitted
Correct answer

76%
Answered correctly

07 secs
Time Spent

02/08/2020
Last Updated

Incidence and prevalence are important concepts for evaluating the impact of disease on a population. **Incidence** corresponds to the number of **new cases** of a disease diagnosed in a population at risk over a given period. **Prevalence** refers to the **total number of diseased individuals** in the population at a particular point; it is dependent on incidence and the average duration of the disease (ie, time from diagnosis to cure or death):

Prevalence = (Incidence) x (Duration of disease)

A simplified diagram compares incidence and prevalence to adding new drops (incident cases) to a sink collecting water (prevalent cases).

The above graph shows that the incidence of type II diabetes mellitus has been constant for the last 30 years **(Choice F)**, but that **prevalence is rising**. Because this is a steady-state population with little migration, a constant incidence rate should result in a nearly stable disease prevalence, unless there is some additional factor affecting the duration of the condition. Factors that **prolong disease duration** can increase disease prevalence even when the incidence is unchanged because diseased individuals live longer on average. In this case, **improved quality of care** likely led to a lower mortality rate in diabetics over time, resulting in a higher prevalence of the disease in the population **(Choice B)**.

(Choice A) A decreased hospitalization rate would indicate reduced morbidity (ie, burden of disease) among diabetic individuals. However, a decrease in hospitalization rate would not necessarily be associated with reduced mortality and increasing disease prevalence.

(Choice D) Increased accuracy of diagnostic testing would affect both the prevalence and incidence of a disease as it changes the rate at which new cases are detected.

(Choice E) Increased exposure to diabetes risk factors would likely increase both disease incidence and prevalence.

(Choice G) Selective survival bias occurs in case-control studies when cases are selected from the entire disease population instead of from just those that are newly diagnosed. For instance, a study on cancer survival that is not limited to newly diagnosed patients could contain a higher proportion of relatively benign malignancies, as these patients generally live longer.

Educational objective:
Prevalence equals the incidence rate multiplied by the average disease duration. Changing disease prevalence in a steady-state population with a constant incidence rate means that there is an additional factor affecting the duration of the condition. A factor that prolongs disease duration (eg, improved quality of care) will increase disease prevalence, as affected patients survive longer.

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A simplified diagram comp

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(Choice D) Increased ac ch new cases are detected.

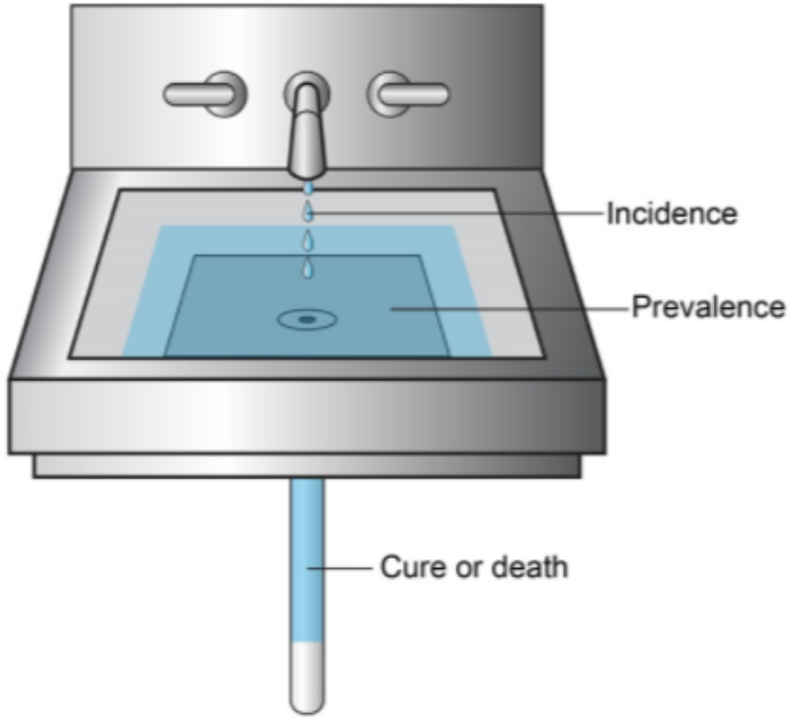
(Choice E) Increased ex

(Choice G) Selective su ust those that are newly diagr proportion of relatively be

Educational objective:
Prevalence equals the inc ith a constant incidence rate h (eg, improved quality of ca

Exhibit Display

Incidence & prevalence



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Prevalence = (Incidence) x (Duration of disease)

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Biostatistics	Biostatistics & Epidemiology	Risk, rate, prevalence and incidence
Subject	System	Topic

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Officials of a public health department report a higher than normal prevalence of acute myelogenous leukemia (AML) among children age 5-12 in their community. They observe that some households in the community are exposed to chemical waste from a nearby factory and worry that exposure to this waste is responsible for the increased prevalence of AML. A case-control study is designed to evaluate the health department officials' claim that exposure to chemical waste is associated with AML in childhood. Which of the following populations should be selected as the control group?

A. Children who do not have AML and are exposed to chemical waste

B. Children who do not have AML and are not exposed to chemical waste

C. Children who do not have AML, regardless of exposure status to chemical waste

D. Children who have AML and are exposed to chemical waste

E. Children who have AML and are not exposed to chemical waste

F. Children who have AML, regardless of exposure status to chemical waste

Submit

Officials of a public health department report a higher than normal prevalence of acute myelogenous leukemia (AML) among children age 5-12 in their community. They observe that some households in the community are exposed to chemical waste from a nearby factory and worry that exposure to this waste is responsible for the increased prevalence of AML. A case-control study is designed to evaluate the health department officials' claim that exposure to chemical waste is associated with AML in childhood. Which of the following populations should be selected as the control group?

A. Children who do not have AML and are exposed to chemical waste (19%)

B. Children who do not have AML and are not exposed to chemical waste (20%)

✓ C. Children who do not have AML, regardless of exposure status to chemical waste (30%)

D. Children who have AML and are exposed to chemical waste (0%)

E. Children who have AML and are not exposed to chemical waste (23%)

F. Children who have AML, regardless of exposure status to chemical waste (4%)

Omitted
Correct answer
C

30%
Answered correctly

02 secs
Time Spent

05/08/2020
Last Updated

Explanation

Case-control study design

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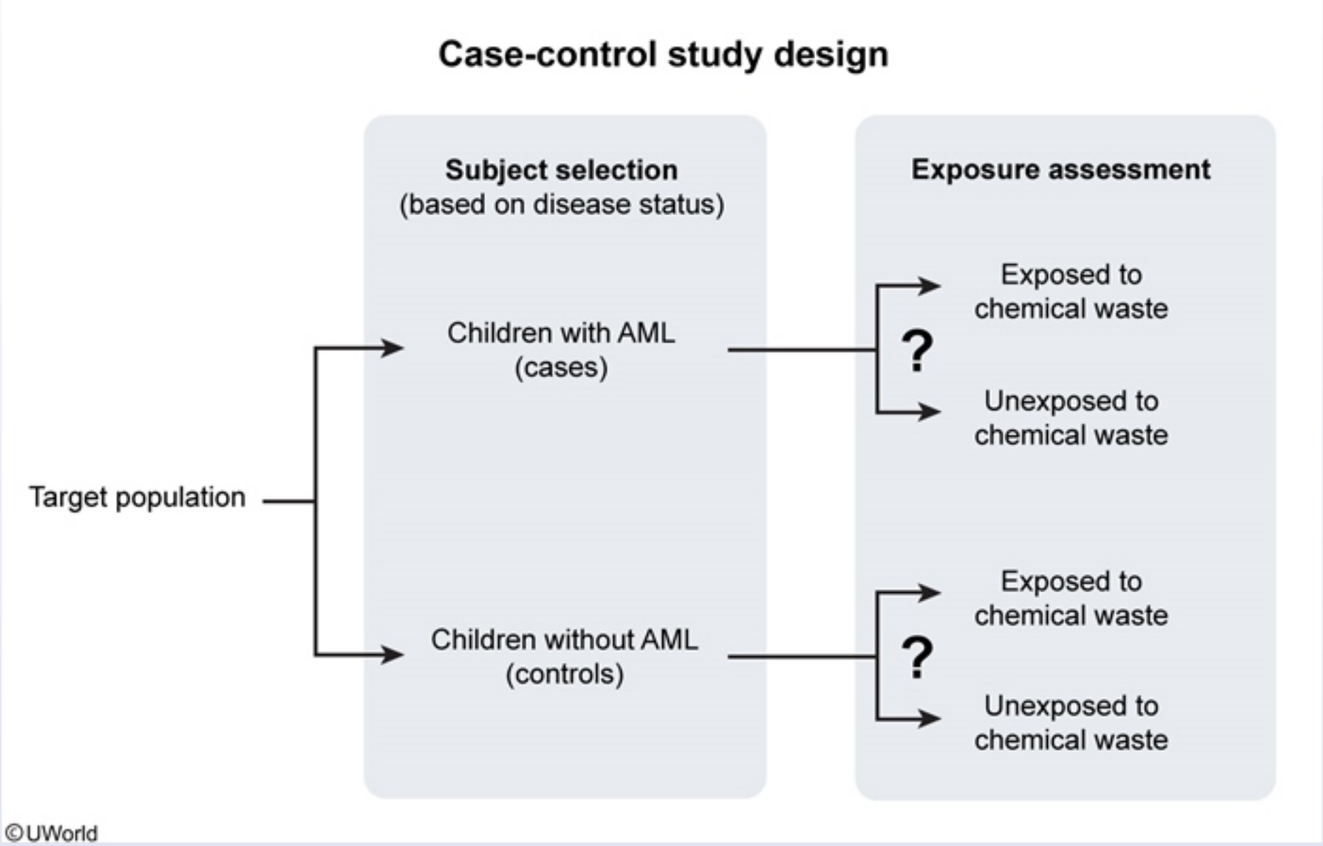

A **case-control study** is the most appropriate study design for evaluating the public health officials' claim. This is because the disease (acute myelogenous leukemia [AML]) is a rare condition occurring at a higher rate in this population, and a retrospective exposure (chemical waste exposure) needs to be evaluated. In case-control studies, 2 groups of subjects are created: **cases** (subjects **with** the disease of interest) and **controls** (subjects **without** the disease of interest). After the case and control groups are selected, exposure frequency to a specific variable (eg, chemical waste) within both groups is ascertained. If there is a statistically significant difference in exposure frequency between the 2 groups, it is likely that the variable in question is associated with disease development.

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A **case-control study** is the most appropriate study design for evaluating the public health officials' claim. This is because the disease (acute myelogenous leukemia [AML]) is a rare condition occurring at a higher rate in this population, and a retrospective exposure (chemical waste exposure) needs to be evaluated. In case-control studies, 2 groups of subjects are created: **cases** (subjects **with** the disease of interest) and **controls** (subjects **without** the disease of interest). After the case and control groups are selected, exposure frequency to a specific variable (eg, chemical waste) within both groups is ascertained. If there is a statistically significant difference in exposure frequency between the 2 groups, it is likely that the variable in question is associated with disease development.

In this example, AML is the disease of interest; therefore, children with AML should be used as cases and children **without AML** should be used as **controls**. Cases and controls should be selected **regardless** of exposure status to the chemical waste **(Choices A and B)**. Selecting subjects based on exposure status is inappropriate because comparing the frequency of exposure between the case and control groups is what determines whether the exposure is more prevalent among cases as compared to controls.

Ideally, exposure frequency among controls should be representative of that among the population of individuals "at risk" of becoming cases. In other words, for a given case-control study, controls are nondiseased individuals who could be considered cases if they had the disease. Often, controls and cases are matched based on independent variables (eg, age, sex) to decrease the effects of confounding.

(Choices D, E, and F) AML is the outcome of interest; therefore, children who have AML can be used only to form the cases group and cannot be used as controls. Cases should also be selected regardless of exposure status.

Educational objective:
Selection of control subjects in case-control studies is intended to provide an accurate estimation of exposure frequency among the nondiseased general population. Cases and controls should be selected based on disease status, not exposure status.

Biostatistics	Biostatistics & Epidemiology	Study designs
Subject	System	Topic

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A research laboratory develops a new serologic test for detecting prostate cancer. The new assay is compared to transrectal ultrasound-guided prostate biopsy to determine sensitivity and specificity parameters. It is found that the test result is negative in 95% of patients who do not have the disease. If the new assay is used on 8 blood samples taken from patients without prostate cancer, what is the probability of all 8 test results coming back negative?

- A. 0.05×8
- B. 0.95×8
- C. 0.05^8
- D. 0.95^8
- E. $1 - 0.05^8$
- F. $1 - 0.95^8$

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- A. 0.05×8 (3%)
- B. 0.95×8 (33%)
- C. 0.05^8 (3%)
- ✓ D. 0.95^8 (35%)
- E. $1 - 0.05^8$ (10%)
- F. $1 - 0.95^8$ (12%)

Omitted
Correct answer
D

35%
Answered correctly

02 secs
Time Spent

01/27/2020
Last Updated

Explanation

Each of the 8 blood sample results is an **independent event** (ie, one patient's result has no impact on another's) with a 0.95 (95%) probability of correctly testing negative and a 0.05 (5%) probability of incorrectly testing positive. To calculate the chance of all 8 tests testing negative, **multiply the probability** of each test returning a negative result:

$$0.95 \times 0.95 \times 0.95 \times 0.95 \times 0.95 \times 0.95 \times 0.95 \times 0.95 = \mathbf{0.95^8}$$

Explanation

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$0.95 \times 0.95 \times 0.95 \times 0.95 \times 0.95 \times 0.95 \times 0.95 \times 0.95 = \mathbf{0.95^8}$

(Choices A and B) The value 0.05 × 8 is equivalent to adding the probability of a sample testing positive 8 times, and 0.95 × 8 is equivalent to adding the probability of a sample testing negative 8 times. However, the combined probability for a series of independent events is calculated using multiplication, not addition. For instance, when flipping a coin twice the probability of getting 2 heads in a row is not 0.5 + 0.5 = 0.5 × 2 = 1 (100%) but rather 0.5 × 0.5 = 0.25 (25%).

(Choice C) The probability of all 8 samples incorrectly testing positive is given by 0.05^8.

(Choices E and F) Overall, 2 outcomes are possible: either all 8 samples will return the same test result or at least 1 sample will test differently. Because the total probability must add up to 1 (100%) and the probability that all 8 samples will return negative is given by 0.95^8, the probability of at least 1 sample testing positive is $1 - 0.95^8$. Conversely, the probability that all 8 samples will return positive is 0.05^8 while the probability of at least 1 sample testing negative is $1 - 0.05^8$.

Educational objective:
If events are independent, the probability that all events will turn out the same is the product of the separate probabilities for each event. The probability of at least 1 event turning out differently is given as 1 - P(all events being the same).

Biostatistics	Biostatistics & Epidemiology	Probability theory
Subject	System	Topic

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The graph below shows the yearly incidence of viral hepatitis per 100,000 population from 1982-2012 in the United States (US).

During this period, the total population in the US continued to increase, as shown in the table below:

Year	1982	1987	1992	1997	2002	2007	2012
US population (in millions)	~230	~243	~258	~275	~290	~303	~315

At any given time point, the number of individuals at risk for hepatitis infection is assumed to be equal to the total US population. Based on these data, which of the following is most likely to be true?

A. After 2006, hepatitis B prevalence surpassed hepatitis A and hepatitis C prevalence

B. In 1987, there were as many individuals with hepatitis A as with hepatitis B in the US

C. In 1989, there were more individuals with hepatitis A than with hepatitis B in the US

D. In 1997, there were more new cases of hepatitis A than of hepatitis B and C combined

E. The number of new cases of hepatitis A diagnosed in 1982 and 1998 were exactly the same

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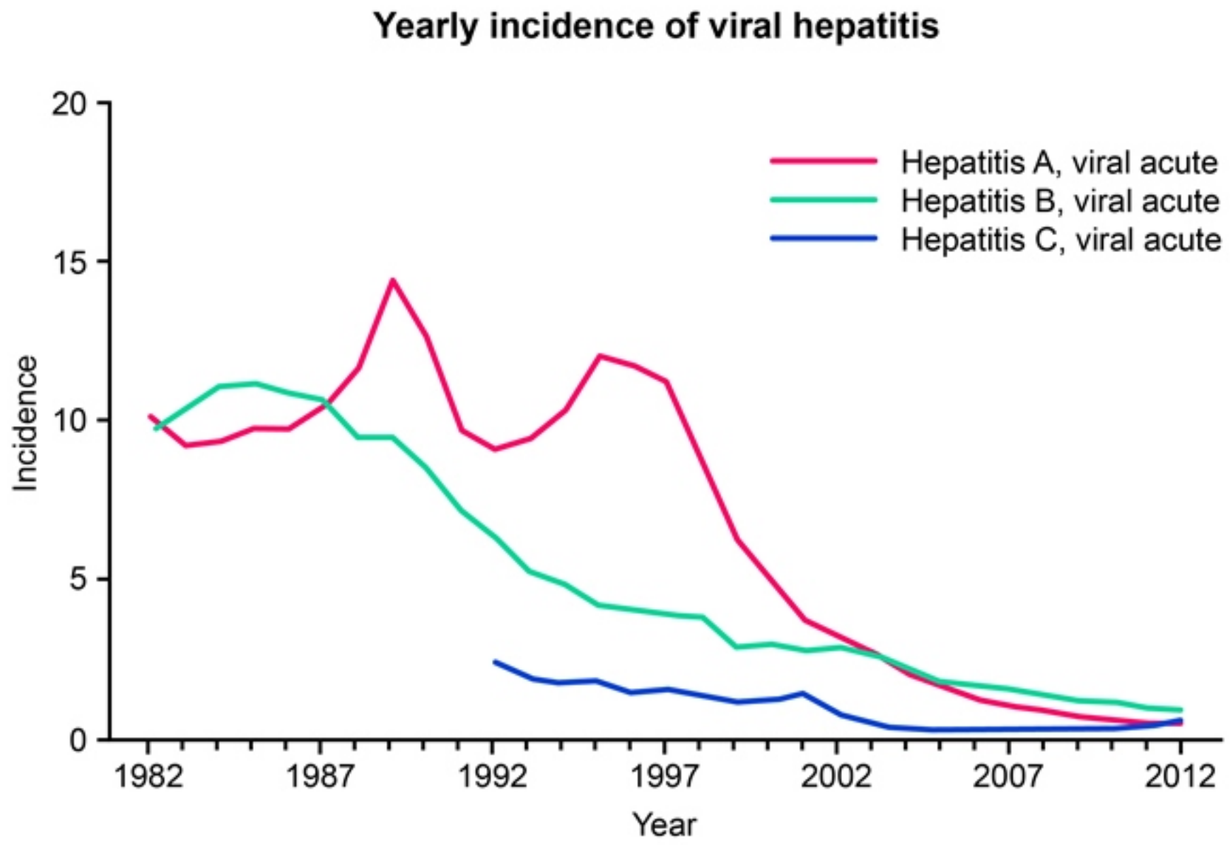

Viral hepatitis incidence (per 100,000 population) in United States, 1982-2012

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During this period, the total population in the US continued to increase, as shown in the table below:

| Year | 1982 | 1987 | 1992 | 1997 | 2002 | 2007 | 2012 |

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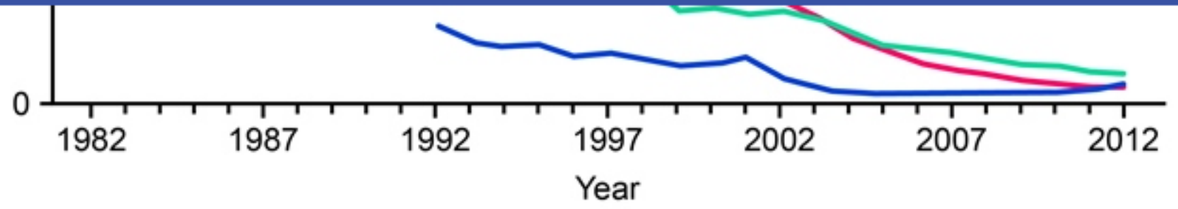

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C. In 1989, there were more individuals with hepatitis A than with hepatitis B in the US

D. In 1997, there were more new cases of hepatitis A than of hepatitis B and C combined

E. The number of new cases of hepatitis A diagnosed in 1982 and 1998 were exactly the same

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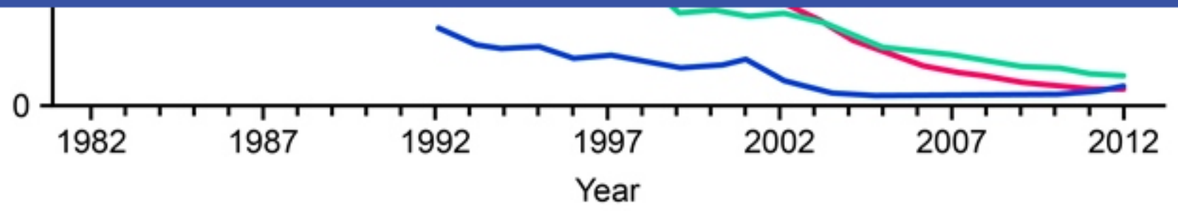

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During this period, the total population in the US continued to increase, as shown in the table below:

Year	1982	1987	1992	1997	2002	2007	2012
US population (in millions)	~230	~243	~258	~275	~290	~303	~315

At any given time point, the number of individuals at risk for hepatitis infection is assumed to be equal to the total US population. Based on these data, which of the following is most likely to be true?

A. After 2006, hepatitis B prevalence surpassed hepatitis A and hepatitis C prevalence (5%)

B. In 1987, there were as many individuals with hepatitis A as with hepatitis B in the US (4%)

C. In 1989, there were more individuals with hepatitis A than with hepatitis B in the US (6%)

✓ D. In 1997, there were more new cases of hepatitis A than of hepatitis B and C combined (78%)

E. The number of new cases of hepatitis A diagnosed in 1982 and 1998 were exactly the same (4%)

Omitted
Correct answer

78%
Answered correctly

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Time Spent

07/07/2020
Last Updated

Incidence corresponds to the number of **new** cases of a disease diagnosed in a population at risk over a given time period. In 1997, incidence was >10 new cases/100,000 population for hepatitis A virus (HAV), <5/100,000 for hepatitis B virus (HBV), and <3/100,000 for hepatitis C virus (HCV). Assuming, as instructed, that the entire United States (US) population is at risk (reasonable theory given low number of hepatitis cases among the total population), then, in 1997 (US population ~275 million):

New HAV cases in 1997 = >10 new cases/100,000 population × 275,000,000 population = >27,500
New HBV cases in 1997 = <5/100,000 × 275,000,000 = <13,750
New HCV cases in 1997 = <3/100,000 × 275,000,000 = <8,250

There were thousands more new HAV (>27,500) than HBV and HCV cases combined (<13,750 + <8,250 = <22,000). The calculations incorporating total population (included for completion) are not needed to answer the question.

After 2006, HBV incidence surpassed HAV and HCV incidence. However, no information can be deduced regarding **prevalence**, which is the **total** number of cases in the population **(Choice A)**. Compared to new HBV cases, there were approximately just as many **new** HAV cases in 1987 and more new HAV cases in 1989. However, the **total** number of HAV or HBV cases in the population cannot be calculated without additional information. In fact, there were likely more total cases (ie, higher prevalence) of HBV as it can progress to a chronic form **(Choices B and C)**.

A simplified diagram compares incidence and prevalence to adding new drops (incident cases) into a water-containing sink (prevalent cases).

(Choice E) HAV incidence **per 100,000 population** was similar in 1982 and 1998. However, the overall US population, and consequently the number of new HAV cases, was different. Assuming HAV incidence was ~10 new cases/100,000 population for both years, then, in 1982 (US population ~230 million):

New HAV cases in 1982 = 10/100,000 × 230,000,000 = 23,000

Also, in 1998 (US population ~275 million at least):

New HAV cases in 1998 = 10/100,000 × 275,000,000 = 27,500

Even with different incidences, it is unlikely that exactly the same number of new HAV diagnoses were made.

After 2006, HBV incidence surpassed HAV and HCV incidence. However, no information can be deduced regarding **prevalence**, which is the **total** number of cases in the population **(Choice A)**. Compared to new HBV cases, there were approximately just as many **new** HAV cases in 1987 and more new HAV cases in 1989. However, the **total** number of HAV or HBV cases in the population cannot be calculated without additional information. In fact, there were likely more total cases (ie, higher prevalence) of HBV as it can progress to a chronic form **(Choices B and C)**.

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New HAV cases in 1982 = 10/100,000 × 230,000,000 = 23,000

Also, in 1998 (US population ~275 million at least):

New HAV cases in 1998 = 10/100,000 × 275,000,000 = 27,500

Even with different incidences, it is unlikely that exactly the same number of new HAV diagnoses were made.

Educational objective:
Incidence corresponds to the number of new cases of a disease in a certain population at risk over a given time period. Prevalence is the total number of cases in the population over a given period.

References

- Summary of notifiable diseases--United States, 2012.

Biostatistics	Biostatistics & Epidemiology	Risk, rate, prevalence and incidence
Subject	System	Topic

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A study is designed to evaluate the efficacy of a new drug, KM28. The study will compare KM28 plus standard care versus standard care alone with regard to decreasing the incidence of recurrent breast cancer. The Food and Drug Administration (FDA) will approve the new drug if KM28 plus standard care decreases the rate of breast cancer recurrence by at least 40% compared to standard therapy alone. The recurrence rate on standard therapy is found to be 8%. In order for the FDA to approve KM28, what is the maximal incidence of recurrent disease acceptable for women treated with KM28 plus standard therapy?

A. 2.8%

B. 3.2%

C. 3.6%

D. 4.8%

E. 5.2%

Submit

A study is designed to evaluate the efficacy of a new drug, KM28. The study will compare KM28 plus standard care versus standard care alone with regard to decreasing the incidence of recurrent breast cancer. The Food and Drug Administration (FDA) will approve the new drug if KM28 plus standard care decreases the rate of breast cancer recurrence by at least 40% compared to standard therapy alone. The recurrence rate on standard therapy is found to be 8%. In order for the FDA to approve KM28, what is the maximal incidence of recurrent disease acceptable for women treated with KM28 plus standard therapy?

- A. 2.8% (2%)
- B. 3.2% (23%)
- C. 3.6% (7%)
- ✓ D. 4.8% (62%)
- E. 5.2% (3%)

Omitted
Correct answer
D

62%
Answered correctly

02 secs
Time Spent

01/24/2020
Last Updated

Explanation

The new drug, KM28, will be approved if its associated recurrence rate is decreased by at least 40% compared to the recurrence rate on standard therapy alone, which is given as 8%. As 40% of 8% is 0.40 × 8% = 3.2%, the maximum acceptable recurrence rate is 8% − 3.2% = 4.8%. Another quick solution would be to state that the maximum acceptable recurrence rate is 60% of 8%, which is 0.60 × 8% = 4.8%.

An alternate solution involves using relative and absolute risk calculations. The 40% (ie, 0.4) mentioned in the prompt refers to **relative risk reduction** (RRR), defined as the percent reduction in absolute risk (AR) between the treatment group (eg, KM28 + standard therapy) and the

Explanation

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An alternate solution involves using relative and absolute risk calculations. The 40% (ie, 0.4) mentioned in the prompt refers to **relative risk reduction** (RRR), defined as the percent reduction in absolute risk (AR) between the treatment group (eg, KM28 + standard therapy) and the control group (eg, standard therapy). The formula for RRR is:

$$RRR = (AR_{control} - AR_{treatment}) / AR_{control}$$

In this example, $AR_{control}$, which represents the risk of recurrence with standard therapy, is given as 8% or 0.08. The formula can be rearranged to calculate $AR_{treatment}$:

$$AR_{treatment} = AR_{control} - (RRR \times AR_{control})$$

Plugging in the values for RRR and $AR_{control}$ gives:

$$AR_{treatment} = 0.08 - (0.4 \times 0.08) = 0.08 - 0.032 = 0.048 \text{ (ie, 4.8\%)}$$

RRR may overstate the effectiveness of an intervention. For example, a RRR of 50% occurs whether a drug decreases the incidence of a disease from 2% to 1% or from 50% to 25%. Clearly, the latter is of greater clinical significance.

Educational objective:
Relative risk reduction = (absolute $risk_{control}$ − absolute $risk_{treatment}$) / absolute $risk_{control}$

Biostatistics	Biostatistics & Epidemiology	Risk
Subject	System	Topic

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Pulmonary capillary wedge pressure (PCWP) measurements can be used to estimate left atrial pressure; the normal range is between 6-12 mm Hg, and recorded values are whole numbers. A patient in the intensive care unit has 20 serial PCWP measurements taken over the course of 2 hours. Among these 20 observations, the maximal recorded value is 12 mm Hg and the minimal recorded value is 10 mm Hg. If the next measurement is 26 mm Hg, which of the following is most likely to remain unchanged?

A. Mean

B. Mode

C. Range

D. Standard deviation

E. Variance

Submit

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A. Mean (3%)
✓ B. Mode (89%)
C. Range (1%)
D. Standard deviation (3%)
E. Variance (1%)

Omitted
Correct answer
B

89%
Answered correctly

02 secs
Time Spent

01/13/2020
Last Updated

Explanation

An **outlier** is defined as an extreme and unusual value observed in a dataset. It may be the result of a recording error, a measurement error, or a natural phenomenon. In this case, the value of 26 mm Hg is an outlier as all the other values lie between 10 and 12 mm Hg. An outlier can affect measures of central tendency (mean, median, mode) as well as measures of dispersion (standard deviation, variance).

This patient had 20 initial measurements that were all between 10 and 12 mm Hg. Although it is not required to answer this question correctly, a numerical example can help to explain the effect of an outlier such as 26 mm Hg. Assume that the patient's 20 initial measurements were: 9 measurements of 10 mm Hg, 6 measurements of 11 mm Hg, and 5 measurements of 12 mm Hg. The **mode** is the most frequently observed data

An **outlier** is defined as an extreme and unusual value observed in a dataset. It may be the result of a recording error, a measurement error, or a natural phenomenon. In this case, the value of 26 mm Hg is an outlier as all the other values lie between 10 and 12 mm Hg. An outlier can affect measures of central tendency (mean, median, mode) as well as measures of dispersion (standard deviation, variance).

This patient had 20 initial measurements that were all between 10 and 12 mm Hg. Although it is not required to answer this question correctly, a numerical example can help to explain the effect of an outlier such as 26 mm Hg. Assume that the patient's 20 initial measurements were: 9 measurements of 10 mm Hg, 6 measurements of 11 mm Hg, and 5 measurements of 12 mm Hg. The **mode** is the most frequently observed data point, so the mode for this initial dataset is 10 mm Hg (because this value is observed 9 times whereas the other 2 values are observed 6 times and 5 times). If the next measurement is 26 mm Hg, the mode would remain 10 mm Hg because this would still be the most commonly observed value. Therefore, the mode would remain unchanged. The mode tends to be resistant to outliers because outliers are not likely to affect the most frequently observed value in a dataset.

(Choice A) The **mean** (or average) can be quite sensitive to outliers, especially in the case of small datasets and extreme outliers. For instance, the mean of the 20 initial measurements is 10.8 mm Hg (obtained by calculating [9 × 10 mm Hg + 6 × 11 mm Hg + 5 × 12 mm Hg] / 20). With an additional measurement of 26 mm Hg, the mean would become 11.5 mm Hg (obtained by calculating [1 × 26 mm Hg + 9 × 10 mm Hg + 6 × 11 mm Hg + 5 × 12 mm Hg] / 21).

(Choice C) The **range** is equal to the maximal value minus the minimal value and would clearly be affected by outliers. With the 20 initial measurements, the range is 12 mm Hg – 10 mm Hg = 2 mm Hg. If the next measurement is 26 mm Hg, then the range will be 26 mm Hg – 10 mm Hg = 16 mm Hg.

(Choices D and E) The standard deviation and variance are measures of dispersion, which reflect how spread out the values in a dataset are from one another. The standard deviation and variance tend to be sensitive to outliers because outliers increase the dispersion of datasets.

Educational objective:
An outlier is defined as an extreme and unusual observed value in a dataset. It can affect measures of central tendency (mean, median, mode) as well as measures of dispersion (standard deviation, variance). Modes tend to be resistant to outliers.

Biostatistics	Biostatistics & Epidemiology	Central tendency (mean, median, mode, outliers)
Subject	System	Topic

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A researcher is interested in studying whether there is an association between neural tube defects and use of acetaminophen during the first 3 months of pregnancy. He randomly chooses a group of women who have just delivered babies with neural tube defects, and a second group of women who delivered apparently healthy babies. These 2 groups were then asked about their use of acetaminophen during the first 3 months of pregnancy. Which of the following measures of association are the investigators most likely to report?

A. Median survival

B. Odds ratio

C. Prevalence ratio

D. Relative rate

E. Relative risk

Submit

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- A. Median survival (0%)
- ✓ B. Odds ratio (59%)
- C. Prevalence ratio (2%)
- D. Relative rate (2%)
- E. Relative risk (34%)

Omitted
Correct answer
B

59%
Answered correctly

02 secs
Time Spent

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Last Updated

Explanation

This scenario describes a typical case-control study design. People with the disease of interest (ie, **cases** [women who have just delivered babies with neural tube defects]) and people without this disease (ie, **controls** [women who delivered apparently healthy babies]) are asked about **previous exposure** to the risk factor being studied (eg, acetaminophen use during the first 3 months of pregnancy). The main measure of association is the **odds ratio (OR)**. The OR can be calculated as follows:

OR = (odds of exposure in cases) / (odds of exposure in controls)

(Choice A) Median survival is calculated in cohort studies or clinical trials, and is usually used to compare the median survival times in >2 groups

Explanation

This scenario describes a typical case-control study design. People with the disease of interest (ie, **cases** [women who have just delivered babies with neural tube defects]) and people without this disease (ie, **controls** [women who delivered apparently healthy babies]) are asked about **previous exposure** to the risk factor being studied (eg, acetaminophen use during the first 3 months of pregnancy). The main measure of association is the **odds ratio (OR)**. The OR can be calculated as follows:

OR = (odds of exposure in cases) / (odds of exposure in controls)

(Choice A) Median survival is calculated in cohort studies or clinical trials, and is usually used to compare the median survival times in ≥2 groups of patients (eg, those receiving a new treatment and those receiving a placebo).

(Choice C) Prevalence ratio is a ratio of 2 probabilities (ie, prevalence) commonly used in cross-sectional studies to compare the prevalence of disease among exposed and unexposed groups of people. In case-control studies, cases and controls are selected from a pool of potential cases and controls that do not represent the real frequency (ie, prevalence) of disease in the population. Therefore, estimating the prevalence of disease in case-control studies would be biased.

(Choices D and E) Incidence measures (eg, relative risk or relative rate) cannot be directly measured in case-control studies because cases, by definition, already have the disease (ie, the study does not follow a cohort for development of a disease). Relative risk and relative rate are calculated in prospective and retrospective cohort studies, where risk factor assessment occurs *first* and then exposed and unexposed groups are followed over time and assessed for development of disease.

Educational objective:
A case-control study is used to compare the exposure status of people with the disease (ie, cases) to the exposure status of people without the disease (ie, controls). The main measure of association is the odds ratio.

Biostatistics	Biostatistics & Epidemiology	Odds ratio
Subject	System	Topic

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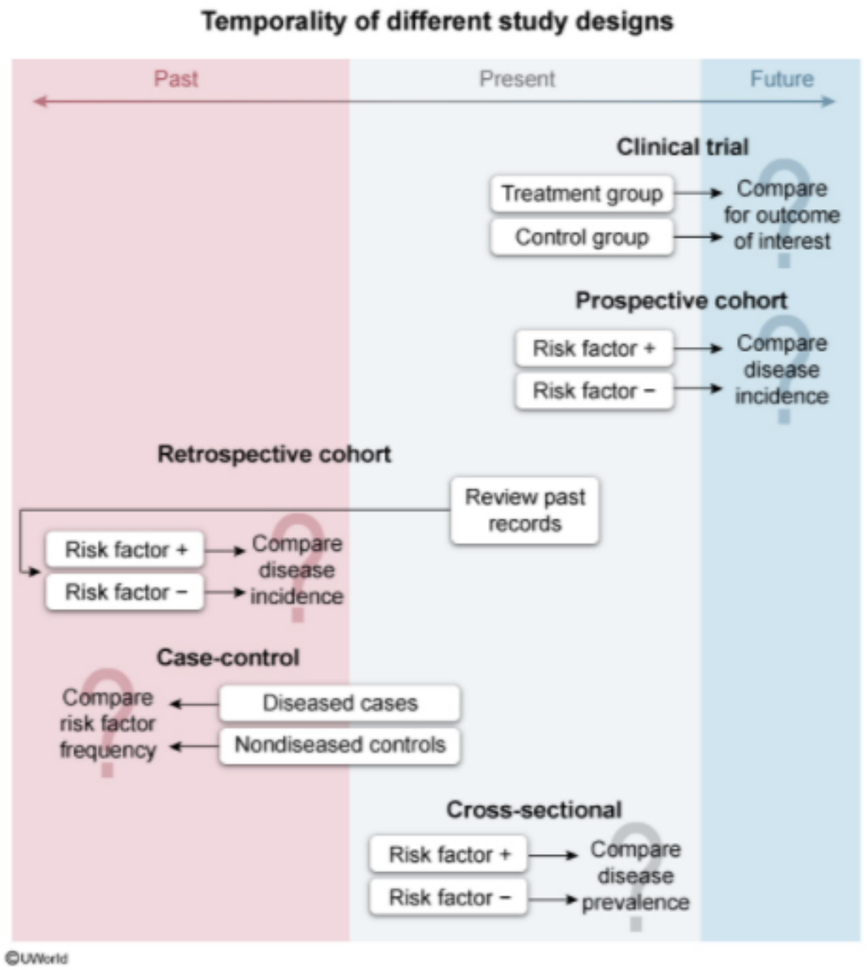
Explanation

Exhibit Display



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A study compared drug A versus standard therapy in preventing recurrent pulmonary embolism (PE). The absolute risk reduction for drug A versus standard therapy was 4%. The incidence of recurrent PE in the standard therapy group was 6%. There were 24 patients who developed recurrent PE in the drug A group. How many total subjects were there in the drug A group?

A. 600
B. 900
C. 1200
D. 1500
E. 1800
F. 2100

Submit

A study compared drug A versus standard therapy in preventing recurrent pulmonary embolism (PE). The absolute risk reduction for drug A versus standard therapy was 4%. The incidence of recurrent PE in the standard therapy group was 6%. There were 24 patients who developed recurrent PE in the drug A group. How many total subjects were there in the drug A group?

- A. 600 (16%)
- B. 900 (6%)
- ✓ C. 1200 (67%)
- D. 1500 (4%)
- E. 1800 (3%)
- F. 2100 (1%)

Omitted
Correct answer
C

67%
Answered correctly

02 secs
Time Spent

01/25/2020
Last Updated

Explanation

This question is meant to challenge your knowledge of how absolute risk reductions (ARR) are calculated. The ARR equals the event rate in the control group ($ER_{control}$) minus the event rate in the treatment group ($ER_{treatment}$). In this example, the event rate represents the incidence of recurrent pulmonary embolism (PE); $ER_{treatment}$ is the incidence of recurrent PE in the drug A group, and $ER_{control}$ is the incidence in the standard therapy group. $ER_{treatment}$ can be determined from the ARR (given as 4%) and $ER_{control}$ (given as 6%):

$$ARR = ER_{control} - ER_{treatment}$$

$$4\% = 6\% - ER$$

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C

Answered correctly | Time Spent | Last Updated

Explanation

This question is meant to challenge your knowledge of how absolute risk reductions (ARR) are calculated. The ARR equals the event rate in the control group ($ER_{control}$) minus the event rate in the treatment group ($ER_{treatment}$). In this example, the event rate represents the incidence of recurrent pulmonary embolism (PE); $ER_{treatment}$ is the incidence of recurrent PE in the drug A group, and $ER_{control}$ is the incidence in the standard therapy group. $ER_{treatment}$ can be determined from the ARR (given as 4%) and $ER_{control}$ (given as 6%):

$ARR = ER_{control} - ER_{treatment}$
$4\% = 6\% - ER_{treatment}$
$ER_{treatment} = 2\% = 0.02$

This value ($ER_{treatment}$) also represents the number of events in the treatment arm divided by the number of subjects in the treatment arm. Therefore, knowing the total number of events in the treatment arm (24 instances of recurrent PE in the drug A group), the number of subjects in the treatment arm can be easily calculated:

$ER_{treatment}$ = Number of events in the treatment arm / Number of subjects in the treatment arm
0.02 = 24 / Number of subjects in the treatment arm
Number of subjects in the treatment arm = 24 / 0.02 = 1200

Educational objective:
Absolute risk reduction = event rate in the control group − event rate in the treatment group.

Biostatistics	Biostatistics & Epidemiology	Risk
Subject	System	Topic

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A 73-year-old man comes to the office for follow-up. He was diagnosed with chronic lymphocytic leukemia (CLL) 3 years ago when routine laboratory testing revealed a markedly elevated leukocyte count. He feels well. On examination, he has stable lymphadenopathy. He has been reading about management options should his CLL progress and inquires about an experimental drug that selectively binds malignant lymphocytes. The drug has been shown to significantly prolong survival in patients with stage 3 and 4 CLL, without curing the malignancy. If this new drug were widely used, what changes would be expected in the number of incident and prevalent cases of CLL?

A. The number of incident cases will decrease, the number of prevalent cases will decrease

B. The number of incident cases will increase, the number of prevalent cases will not change

C. The number of incident cases will decrease, the number of prevalent cases will increase

D. The number of incident cases will not change, the number of prevalent cases will increase

E. The number of incident cases will not change, the number of prevalent cases will not change

Submit

A 73-year-old man comes to the office for follow-up. He was diagnosed with chronic lymphocytic leukemia (CLL) 3 years ago when routine laboratory testing revealed a markedly elevated leukocyte count. He feels well. On examination, he has stable lymphadenopathy. He has been reading about management options should his CLL progress and inquires about an experimental drug that selectively binds malignant lymphocytes. The drug has been shown to significantly prolong survival in patients with stage 3 and 4 CLL, without curing the malignancy. If this new drug were widely used, what changes would be expected in the number of incident and prevalent cases of CLL?

A. The number of incident cases will decrease, the number of prevalent cases will decrease (0%)

B. The number of incident cases will increase, the number of prevalent cases will not change (1%)

C. The number of incident cases will decrease, the number of prevalent cases will increase (1%)

✓ D. The number of incident cases will not change, the number of prevalent cases will increase (91%)

E. The number of incident cases will not change, the number of prevalent cases will not change (4%)

Omitted
Correct answer
D

91%
Answered correctly

02 secs
Time Spent

04/20/2020
Last Updated

Explanation

Incident cases represent **new cases** diagnosed in a given period of time. **Prevalent cases** are the **total number of cases** (both old and new) at a particular point in time. For a non-transmissible condition such as chronic lymphocytic leukemia (CLL), the number of incident cases will **not** be changed by any kind of treatment because the disease has already developed when the treatment is started (and treatment of existing patients will not prevent new patients from developing CLL). Any treatment that prolongs survival but does not cure the disease will **increase** the number of prevalent cases due to an increase in the number of afflicted (but still living) individuals over time.

Omitted
Correct answer
D

91%
Answered correctly

02 secs
Time Spent

04/20/2020
Last Updated

Explanation

Incident cases represent **new cases** diagnosed in a given period of time. **Prevalent cases** are the **total number of cases** (both old and new) at a particular point in time. For a non-transmissible condition such as chronic lymphocytic leukemia (CLL), the number of incident cases will **not** be changed by any kind of treatment because the disease has already developed when the treatment is started (and treatment of existing patients will not prevent new patients from developing CLL). Any treatment that prolongs survival but does not cure the disease will **increase** the number of prevalent cases due to an increase in the number of afflicted (but still living) individuals over time.

Differences in terminology may lead to confusion. Incident cases and prevalent cases are often referred to as simply "incidence" and "prevalence." Incidence can also represent the number of new cases divided by the population at risk over a period of time and can be converted into a rate (eg, annual incidence per 10,000 population). Prevalence typically refers to point prevalence (total number of cases at a particular point in time) as opposed to period prevalence (over a period of time). The specific meaning is often clear from the context.

Educational objective:
Incident cases represent new cases diagnosed in a given period of time. Prevalent cases are the total number of cases (both old and new) at a particular point in time. Any treatment that prolongs survival but does not cure the disease will increase prevalence due to an increase in the number of afflicted (but still living) individuals over time.

Biostatistics	Biostatistics & Epidemiology	Risk, rate, prevalence and incidence
Subject	System	Topic

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A large, multi-country study is conducted to determine the effect of economic development on cancer incidence and mortality. The study uses data obtained from the national cancer registries, along with information regarding per capita gross domestic product as reported by the International Monetary Fund and life expectancy as reported by the World Health Organization. Which of the following best describes the design of this study?

A. Case-control study
B. Cohort study
C. Cross-sectional survey
D. Ecological study
E. Nested case-control study
F. Qualitative study
G. Randomized controlled trial
H. Systematic review

Submit

A large, multi-country study is conducted to determine the effect of economic development on cancer incidence and mortality. The study uses data obtained from the national cancer registries, along with information regarding per capita gross domestic product as reported by the International Monetary Fund and life expectancy as reported by the World Health Organization. Which of the following best describes the design of this study?

- A. Case-control study (4%)
- B. Cohort study (7%)
- C. Cross-sectional survey (28%)
- ✓ D. Ecological study (35%)
- E. Nested case-control study (1%)
- F. Qualitative study (4%)
- G. Randomized controlled trial (0%)
- H. Systematic review (18%)

Omitted
Correct answer
D

35%
Answered correctly

02 secs
Time Spent

02/03/2020
Last Updated

Explanation

This observational study is analyzing **population-level data** to evaluate the association between a potential exposure (eg, low socioeconomic status population) and a given outcome (eg, increased cancer mortality). Using population-level (rather than individual-level) data as a unit of

Explanation

This observational study is analyzing **population-level data** to evaluate the association between a potential exposure (eg, low socioeconomic status population) and a given outcome (eg, increased cancer mortality). Using population-level (rather than individual-level) data as a unit of analysis in such a manner is consistent with an **ecological study**. Ecological studies are useful for generating hypotheses but should not be used to draw conclusions regarding individuals within these populations (**ecological fallacy**).

(Choices A and B) Case-control and cohort studies deal with *individuals* rather than populations. In case-control studies, the odds of exposure to a certain characteristic (eg, personal socioeconomic status) are compared between affected individuals (eg, patients with cancer) and unaffected individuals who serve as controls. In cohort studies, individuals with and without different exposures (eg, high or low personal socioeconomic status) are followed over time to determine the incidence of the disease of interest (eg, cancer).

(Choice C) Cross-sectional surveys evaluate the exposures and outcomes of interest in individuals (not populations) at a given point in time ("snapshot"). The overall design of this multi-country study relies on population-level data, not individual-level data.

(Choice E) Nested case-control studies start with cohort studies in which participants are followed over time; those participants who develop an outcome of interest become cases for a case-control study.

(Choice F) Qualitative studies use focus groups, interviews (structured and semi-structured), and other anthropologic techniques to obtain narrative information for explaining quantitative results.

(Choice G) Randomized controlled trials randomly assign subjects into a treatment group or a control group. The groups differ only in the intervention (treatment) of interest.

(Choice H) Systematic reviews and meta-analyses combine the results of several published studies (with an emphasis on high-quality, randomized controlled studies) to estimate the pooled effect.

Educational objective:
The unit of analysis in ecological studies is populations rather than individuals.

Biostatistics	Biostatistics & Epidemiology	Study designs
Subject	System	Topic

status population) and a given outcome (eg, increased cancer mortality). Using population-level (rather than individual-level) data as a unit of analysis in such a manner is consistent with an **ecological study**. Ecological studies are useful for generating hypotheses but should not be used to draw conclusions regarding individuals within these populations (**ecological fallacy**).

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Biostatistics	Biostatistics & Epidemiology	Study designs
Subject	System	Topic

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The results of a study investigating a new diagnostic test for acute myocardial infarction (MI) are given in the table below.

	MI	No MI
Test positive	75	20
Test negative	25	80

What is the sensitivity of the new diagnostic test?

A. 25%
B. 37.5%
C. 50%
D. 75%
E. 79%
F. 80%

Submit

The results of a study investigating a new diagnostic test for acute myocardial infarction (MI) are given in the table below.

	MI	No MI
Test positive	75	20
Test negative	25	80

What is the sensitivity of the new diagnostic test?

- A. 25% (1%)
- B. 37.5% (0%)
- C. 50% (0%)
- ✓ D. 75% (88%)
- E. 79% (5%)
- F. 80% (2%)

Omitted
Correct answer
D

88%
Answered correctly

02 secs
Time Spent

07/04/2020
Last Updated

Explanation

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	Positive condition	Negative condition	
Positive test result	TP	FP	PPV = TP/(TP + FP)
Negative test result	FN	TN	NPV = TN/(TN + FN)
	Sensitivity = TP/(TP + FN)	Specificity = TN/(TN + FP)	

FN = false negative; **FP** = false positive; **NPV** = negative predictive value; **PPV** = positive predictive value; **TN** = true negative; **TP** = true positive.

The data is presented in the standard 2 × 2 (contingency) table format. The **sensitivity** of a test refers to its ability to correctly identify individuals affected with a disease. It is the number of true positives divided by the total number of patients with the disease. Sensitivity should be high in screening tests in order to pick up all cases of a disease (decrease false negatives). Using the generic 2 × 2 (contingency) table:

Sensitivity = TP / (TP + FN), where TP is true positives and FN is false negatives. In this case:

Sensitivity = 75 / (75 + 25) = 75/100 = 0.75 (or 75%)

(Choice A) The false negative rate is (1 – sensitivity) = 1 – 0.75 = 0.25 (or 25%). The false negative rate is not affected by disease prevalence.

(Choice B) The value 37.5% is obtained by dividing the TP (75) by the total number of patients in the study (75 + 25 + 20 + 80 = 200).

(Choice C) The number of patients with myocardial infarction (MI) based on the gold standard is 100 (= 75 + 25). The total number of patients in the study is 200 (= 75 + 25 + 20 + 80). Therefore, the prevalence of MI in this sample is 100/200 = 0.5 (or 50%).

(Choice E) The positive predictive value (PPV) of the test (the probability that a person has the disease given a positive test result) is given by: PPV = TP / (TP + FP), where FP is false positives. In this case, PPV = 75 / (75 + 20) = 75/95 = 0.79 (or 79%).

TP/(TP + FN)	TN/(TN + FP)

FN = false negative; **FP** = false positive; **NPV** = negative predictive value; **PPV** = positive predictive value; **TN** = true negative; **TP** = true positive.

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(Choice E) The positive predictive value (PPV) of the test (the probability that a person has the disease given a positive test result) is given by: PPV = TP / (TP + FP), where FP is false positives. In this case, PPV = 75 / (75 + 20) = 75/95 = 0.79 (or 79%).

(Choice F) The test specificity (its ability to correctly identify individuals without the disease) is 80 / (80 + 20) = 80/100 = 0.80 (or 80%).

Educational objective:
Sensitivity = true positives / (true positives + false negatives). Screening tests should have high sensitivity.

Biostatistics	Biostatistics & Epidemiology	Sensitivity, specificity, positive predictive value PPV, negative predictive value NPV
Subject	System	Topic

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A new estrogen receptor agonist is being evaluated for the treatment of postmenopausal symptoms. A prospective study shows that the drug increases the risk of deep vein thrombosis (DVT) in treated women who smoke compared to untreated women who smoke, with a relative risk (RR) of 1.70 and p-value of 0.01. In nonsmokers, no increased risk of DVT is evident with use of the drug (RR = 0.96; p-value = 0.68). Which of the following describes this phenomenon?

A. Confounding
B. Effect modification
C. Latent period
D. Observer bias
E. Selection bias

Submit

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- A. Confounding (48%)
- ✓ B. Effect modification (40%)
- C. Latent period (2%)
- D. Observer bias (2%)
- E. Selection bias (6%)

Omitted
Correct answer
B

40%
Answered correctly

02 secs
Time Spent

01/24/2020
Last Updated

Explanation

Effect modification occurs when the effect of an exposure on an outcome is modified by another variable. It can be identified using **stratified analysis** (analyzing the cohort as different subgroups), as the different strata will have **different measures of association**. In this scenario, smoking status modified the effect of the new estrogen receptor agonist (exposure) on deep vein thrombosis (DVT) incidence (outcome). Using stratified analysis by smoking status:

- Among smokers, there was a statistically significant association between taking the new estrogen receptor agonist and risk of developing DVT with a relative risk of >1, indicating higher risk, and a p-value of <0.05, indicating statistical significance.

Effect modification occurs when the effect of an exposure on an outcome is modified by another variable. It can be identified using **stratified analysis** (analyzing the cohort as different subgroups), as the different strata will have **different measures of association**. In this scenario, smoking status modified the effect of the new estrogen receptor agonist (exposure) on deep vein thrombosis (DVT) incidence (outcome). Using stratified analysis by smoking status:

- Among smokers, there was a statistically significant association between taking the new estrogen receptor agonist and risk of developing DVT with a relative risk of >1, indicating higher risk, and a p-value of <0.05, indicating statistical significance.
- In contrast, among nonsmokers, there was no statistically significant association between taking the medication and risk of DVT (p-value >0.05).

Effect modification is not a bias **(Choices D and E)**, as it is not due to flaws in the design or analysis phases of the study. It is a natural phenomenon that should be described, not corrected.

Effect modification is most easily confused with **confounding (Choice A)**, but stratified analysis can help distinguish between these 2 scenarios. With effect modification, the different strata will have different measures of association, as seen in this example of the association between taking the estrogen receptor and the risk of DVT among smokers compared to nonsmokers. In contrast, with confounding, stratification usually reveals no significant difference between the strata. For instance, in an analysis of primary school students (of all grade levels), age can be a confounder that muddies the association between shoe size and intelligence. Children with bigger shoe sizes may appear to be more intelligent on initial analysis. However, this association is likely not due to shoe size but rather to age because older children tend to have both bigger feet and more intelligence. When older and younger children are analyzed separately (stratification based on the confounder), the association between shoe size and intelligence disappears.

(Choice C) The latent period is the time required for an exposure to begin having an effect. However, there is no information on how latency was handled in this study.

Educational objective:
Effect modification is present when the effect of the main exposure on the outcome is modified by the presence of another variable. Effect modification is not a bias.

Biostatistics Biostatistics & Epidemiology Confounding, effect modification, bias, errors

A large study of serum folate levels in a sample of women age 16-45 reveals that this parameter is normally distributed with a mean of 5.0 ng/mL and a standard deviation of 0.5 ng/mL. According to the study results, 95% of serum folate observations in these patients will lie approximately between which of the following limits?

A. 3.5 and 6.0 ng/mL

B. 3.5 and 6.5 ng/mL

C. 4.0 and 6.0 ng/mL

D. 4.0 and 5.5 ng/mL

E. 4.5 and 5.5 ng/mL

Submit

A large study of serum folate levels in a sample of women age 16-45 reveals that this parameter is normally distributed with a mean of 5.0 ng/mL and a standard deviation of 0.5 ng/mL. According to the study results, 95% of serum folate observations in these patients will lie approximately between which of the following limits?

A. 3.5 and 6.0 ng/mL (0%)

B. 3.5 and 6.5 ng/mL (5%)

✓ C. 4.0 and 6.0 ng/mL (79%)

D. 4.0 and 5.5 ng/mL (1%)

E. 4.5 and 5.5 ng/mL (12%)

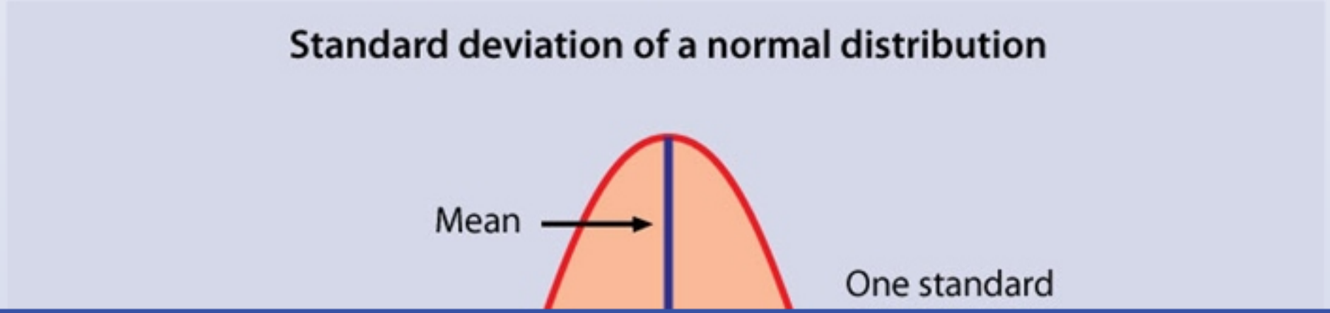
Omitted
Correct answer
C

79%
Answered correctly

01 sec
Time Spent

01/13/2020
Last Updated

Explanation



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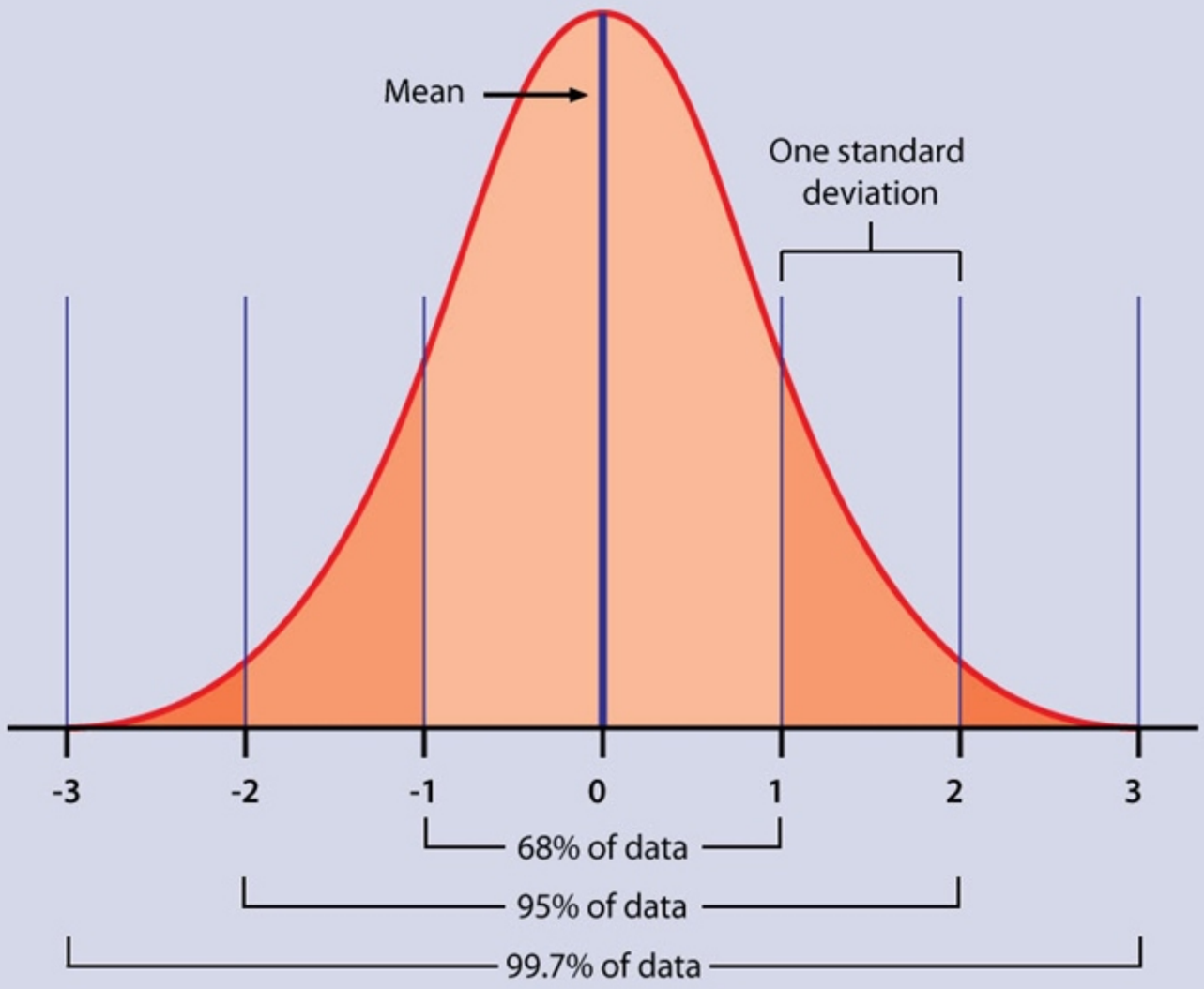
Standard deviation of a normal distribution



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A **normal (Gaussian) distribution** is defined as a symmetrical, bell-shaped distribution curve. One of the most important attributes of the normal distribution is the **"68/95/99 rule,"** which states that 68% of all observations lie within 1 standard deviation (SD) of the mean, 95% within 2 SDs of the mean, and 99.7% within 3 SDs of the mean. The SD is a measure of dispersion or variance (how far the measurements are from one another). In this example, the mean folate level is 5.0 ng/mL with a SD of 0.5 ng/mL. Therefore:

- 4.5-5.5 ng/mL is the range within +/- 1 SD of 5.0 ng/mL (given that 5.0 – 1*0.5 = 4.5 ng/mL and 5 + 1*0.5 = 5.5 ng/mL);
- 4.0-6.0 ng/mL is the range within +/- 2 SDs of 5.0 ng/mL (given that 5.0 – 2*0.5 = 4.0 ng/mL and 5.0 + 2*0.5 = 6.0 ng/mL)
- 3.5-6.5 ng/mL is the range within +/- 3 SDs of 5.0 ng/mL (given that 5.0 – 3*0.5 = 3.5 ng/mL and 5.0 + 3*0.5 = 6.5 ng/mL)

Based on the 68/95/99 rule, approximately 95% of observations lie within 2 SDs of the mean, so between 4.0 and 6.0 ng/mL in this case. These are helpful approximations; to be more precise, 95% of the observations lie within 1.96 SDs of the mean and 95.45% of the observations lie within 2 SDs of the mean.

Note that SD is used to describe individual observations in a dataset. A closely related measure called standard error (SE) is used to show how closely sample means are related to population means; SE = SD / $\sqrt{n}$, where n is the sample size. In this example, if SE had been given instead of SD, investigators would be 95% confident that the true mean folate level in the underlying population lies within the mean +/- 2 SE (which is also the range that would include 95% of sample means calculated from repeated samples of the same size taken from that population).

(Choices A and D) These limits are asymmetric and are therefore inconsistent with a normal distribution curve around the mean.

(Choice B) Approximately 99.7% of all observations lie within 3 SDs of the mean (3.5-6.5 ng/mL).

(Choice E) Approximately 68% of all observations lie within 1 SD of the mean (4.5-5.5 ng/mL).

Educational objective:
In a normal (bell-shaped) distribution curve, 68% of observations lie within 1 standard deviation (SD) of the mean, 95% of observations lie within 2 SDs of the mean, and 99.7% of observations lie within 3 SDs of the mean.

Biostatistics	Biostatistics & Epidemiology	Normal distribution
Subject	System	Topic

distribution is the **"68/95/99 rule,"** which states that 68% of all observations lie within 1 standard deviation (SD) of the mean, 95% within 2 SDs of the mean, and 99.7% within 3 SDs of the mean. The SD is a measure of dispersion or variance (how far the measurements are from one another). In this example, the mean folate level is 5.0 ng/mL with a SD of 0.5 ng/mL. Therefore:

- 4.5-5.5 ng/mL is the range within +/- 1 SD of 5.0 ng/mL (given that 5.0 – 1*0.5 = 4.5 ng/mL and 5 + 1*0.5 = 5.5 ng/mL);
- 4.0-6.0 ng/mL is the range within +/- 2 SDs of 5.0 ng/mL (given that 5.0 – 2*0.5 = 4.0 ng/mL and 5.0 + 2*0.5 = 6.0 ng/mL)
- 3.5-6.5 ng/mL is the range within +/- 3 SDs of 5.0 ng/mL (given that 5.0 – 3*0.5 = 3.5 ng/mL and 5.0 + 3*0.5 = 6.5 ng/mL)

Based on the 68/95/99 rule, approximately 95% of observations lie within 2 SDs of the mean, so between 4.0 and 6.0 ng/mL in this case. These are helpful approximations; to be more precise, 95% of the observations lie within 1.96 SDs of the mean and 95.45% of the observations lie within 2 SDs of the mean.

Note that SD is used to describe individual observations in a dataset. A closely related measure called standard error (SE) is used to show how closely sample means are related to population means; SE = SD / √n, where n is the sample size. In this example, if SE had been given instead of SD, investigators would be 95% confident that the true mean folate level in the underlying population lies within the mean +/- 2 SE (which is also the range that would include 95% of sample means calculated from repeated samples of the same size taken from that population).

(Choices A and D) These limits are asymmetric and are therefore inconsistent with a normal distribution curve around the mean.

(Choice B) Approximately 99.7% of all observations lie within 3 SDs of the mean (3.5-6.5 ng/mL).

(Choice E) Approximately 68% of all observations lie within 1 SD of the mean (4.5-5.5 ng/mL).

Educational objective:
In a normal (bell-shaped) distribution curve, 68% of observations lie within 1 standard deviation (SD) of the mean, 95% of observations lie within 2 SDs of the mean, and 99.7% of observations lie within 3 SDs of the mean.

Biostatistics	Biostatistics & Epidemiology	Normal distribution
Subject	System	Topic

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A study is conducted to assess the effect of beta-blocker therapy in patients with acute myocardial infarction (MI). The study found that 20 patients out of 90 who took a beta-blocker during the week prior to developing an MI had a major arrhythmia event during hospitalization. The study also determined that 30 patients out of 70 who did not take any beta-blocker developed a major arrhythmia. What was the odds ratio of developing major arrhythmia in patients who took beta-blockers compared to those who did not take beta-blockers?

- A. (20 × 30) / (70 × 40)
- B. (20 × 40) / (70 × 30)
- C. (20 × 70) / (30 × 40)
- D. (20 / 50) / (70 / 110)
- E. (20 / 90) / (30 / 70)

Submit

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- A. (20 × 30) / (70 × 40) (5%)
- ✓ B. (20 × 40) / (70 × 30) (53%)
- C. (20 × 70) / (30 × 40) (6%)
- D. (20 / 50) / (70 / 110) (2%)
- E. (20 / 90) / (30 / 70) (32%)

Omitted
Correct answer
B

53%
Answered correctly

01 sec
Time Spent

01/22/2020
Last Updated

Explanation

The odds of an event occurring are defined as the probability of that event happening divided by the probability of the event not happening. For instance, when rolling dice, the probability of rolling a one is 1/6, whereas the probability of rolling any other number is 5/6. Therefore, the odds of rolling a one are 1/5.

The **odds ratio (OR)** is a measure of association that compares the odds of an outcome occurring based on exposure status. In this case, it represents the odds that the outcome (eg, major arrhythmia) occurred in the presence of the exposure (eg, beta blocker use) compared with the odds that the outcome occurred in the absence of that exposure. The OR can be calculated using a standard contingency table (with exposures in

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	Major arrhythmia	**No arrhythmia**	
Beta blocker (exposed group)	20 (a)	70 (b)	90
No beta blocker (unexposed group)	30 (c)	40 (d)	70
	50	110	

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Odds of developing major arrhythmia in exposed group = 20/70
Odds of developing major arrhythmia in unexposed group = 30/40
(note that the total number of people in the exposed and unexposed groups is **not** used to calculate odds, unlike calculating probabilities)

Therefore, the OR of developing a major arrhythmia in patients who took beta blockers compared with those who did not is as follows:

$$(a/b) / (c/d) = (20/70) / (30/40) = \mathbf{(20 \times 40) / (70 \times 30)} = 0.38$$

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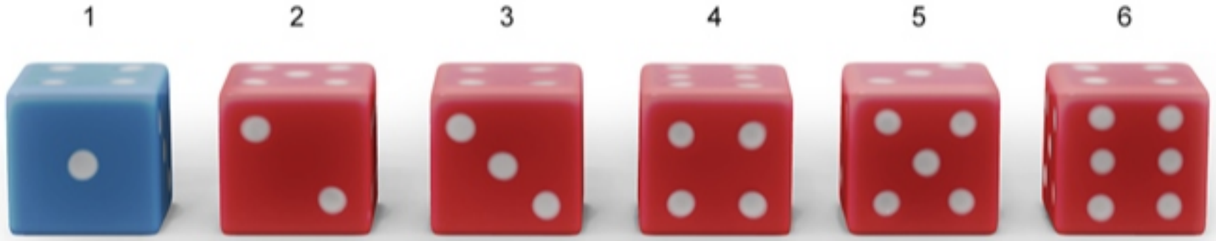
Exhibit Display

Odds vs. probability



Probability of rolling 1: 1/6

Odds of rolling 1: (1/6) / (5/6) = 1/5

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	50	110	

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Odds of developing major arrhythmia in exposed group = 20/70
Odds of developing major arrhythmia in unexposed group = 30/40
(note that the total number of people in the exposed and unexposed groups is **not** used to calculate odds, unlike calculating probabilities)

Therefore, the OR of developing a major arrhythmia in patients who took beta blockers compared with those who did not is as follows:

$$(a/b) / (c/d) = (20/70) / (30/40) = \mathbf{(20 \times 40) / (70 \times 30)} = 0.38$$

In this case, the OR calculated was the OR of disease (among exposed individuals relative to nonexposed individuals), given by (a/b) / (c/d); in some cases, the OR of exposure (among diseased individuals relative to nondiseased individuals) is calculated, given by (a/c) / (b/d). Both OR definitions are mathematically equivalent and reduce (by a mathematical shortcut) to: OR = ad/bc. Any of these formulas would give the same result.

Because the OR is <1, the odds of developing a major arrhythmia is lower for patients who were taking beta blockers compared with those who were not.

(Choice E) Relative risk (RR) is the probability of an outcome occurring in the exposed group compared with the probability of the outcome occurring in the unexposed group. It is calculated using the following formula:

$$RR = [a/(a + b)] / [c/(c + d)] = (20/90) / (30/70)$$

RR often has more clinical utility than the OR since it gives the change in disease risk based on the presence or absence of risk factors. However, RR cannot be calculated in case-control studies as patients are preselected based on disease status (cases and controls) instead of being sorted into exposure groups and followed over time to assess disease outcomes.

Educational objective:
The odds ratio (OR) is a measure of the strength of an association between an exposure and an outcome. Specifically, it represents the odds that an outcome occurred in the presence of a particular exposure compared with the odds that the outcome occurred in the absence of that

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Exhibit Display

Odds ratio calculation in a cohort study

	Diseased	Non-diseased
Exposed	a	b
Non-exposed	c	d

$$\text{OR} = \frac{\text{odds of disease among exposed}}{\text{odds of disease among non-exposed}} = \frac{\dfrac{\text{P(diseased among exposed)}}{\text{1-P(disease among exposed)}}}{\dfrac{\text{P(disease among non-exposed)}}{\text{1-P(disease among non-exposed)}}} = \frac{\dfrac{a/(a+b)}{1-a/(a+b)}}{\dfrac{c/(c+d)}{1-c/(c+d)}} = \frac{a}{b}/\frac{c}{d} = \frac{\mathbf{ad}}{\mathbf{bc}}$$

OR = Odds ratio; P = Probability.

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Therefore, the OR of developing a major arrhythmia in patients who took beta blockers compared with those who did not is as follows:

$$(a/b) / (c/d) = (20/70) / (30/40) = \mathbf{(20 \times 40) / (70 \times 30)} = 0.38$$

In this case, the OR calculated was the OR of disease (among exposed individuals relative to nonexposed individuals), given by (a/b) / (c/d); in some cases, the OR of exposure (among diseased individuals relative to nondiseased individuals) is calculated, given by (a/c) / (b/d). Both OR definitions are mathematically equivalent and reduce (by a mathematical shortcut) to: OR = ad/bc. Any of these formulas would give the same result.

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RR often has more clinical utility than the OR since it gives the change in disease risk based on the presence or absence of risk factors. However, RR cannot be calculated in case-control studies as patients are preselected based on disease status (cases and controls) instead of being sorted into exposure groups and followed over time to assess disease outcomes.

Educational objective:
The odds ratio (OR) is a measure of the strength of an association between an exposure and an outcome. Specifically, it represents the odds that an outcome occurred in the presence of a particular exposure compared with the odds that the outcome occurred in the absence of that exposure. In a standard contingency table, OR = ad/bc.

Biostatistics	Biostatistics & Epidemiology	Odds ratio
Subject	System	Topic

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A researcher studying physician behavior is interested in how often primary care physicians take the sexual histories of patients during clinic visits. As part of the study, patients who attend a primary care clinic are asked to fill out a questionnaire immediately following a visit with their physician. Once the physicians become aware that their own behavior is being studied, which of the following is most likely to be a potential problem?

A. Berkson's bias
B. Hawthorne effect
C. Lead-time bias
D. Pygmalion effect
E. Recall bias

Submit

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- A. Berkson's bias (9%)
- ✓ B. Hawthorne effect (69%)
- C. Lead-time bias (2%)
- D. Pygmalion effect (15%)
- E. Recall bias (2%)

Omitted
Correct answer
B

69%
Answered correctly

01 sec
Time Spent

01/24/2020
Last Updated

Explanation

The **Hawthorne effect (observer effect)** is the tendency of study subjects to change their behavior as a result of their awareness that they are being studied. This can impact the observed outcomes, thereby seriously affecting the validity of the study. The Hawthorne effect is commonly seen in studies concerning behavioral outcomes or outcomes that can be influenced by behavioral changes. In this example, physicians (not patients) are the subjects of the study; those physicians who are aware that they are being studied may modify their behavior and start taking sexual histories. To minimize the Hawthorne effect, study subjects can be kept unaware that they are being studied, but this can occasionally pose ethical problems.

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(Choice A) Berkson's bias refers to selection bias created by choosing hospitalized patients as the control group.

(Choice C) Lead-time bias refers to the apparent prolongation of survival after applying a screening test that detects a disease earlier than it would have been otherwise detected but without any real effect on prognosis.

(Choice D) Pygmalion effect describes the fact that a researcher's beliefs in the efficacy of treatment can potentially affect the outcome. In the classic classroom experiment that first described the Pygmalion effect, a group of students were randomly assigned high intelligence quotient (IQ) scores; their teachers were then told of these artificial results and had higher expectations of this group as a result. The students with the randomly assigned high IQ scores actually performed better, likely because their teachers unconsciously behaved in a manner that would facilitate their success.

(Choice E) Recall bias results from inaccurate recall of past exposures by patients. Although recall bias is possible whenever questionnaires are administered, it is unlikely in this case as the patients fill out a form immediately upon leaving the doctor's office.

Educational objective:
The Hawthorne effect (observer effect) is the tendency of study subjects to change their behavior as a result of their awareness that they are being studied.

Biostatistics	Biostatistics & Epidemiology	Bias
Subject	System	Topic

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Researchers conduct a prospective study that demonstrates an association between alcohol consumption and transitional bladder carcinoma, with a relative risk (RR) of 1.81 and a p-value of 0.03. They then divide the study subjects into 2 groups, smokers and non-smokers, and again examine the association between alcohol consumption and bladder cancer:

	RR	P-value
Smokers	0.95	0.87
Non-smokers	1.03	0.96

The discrepancy between the overall results and the stratified results is best explained by which of the following?

A. Confounding
B. Effect modification
C. Measurement bias
D. Meta-analysis
E. Observer bias
F. Recall bias

Submit

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	RR	P-value
Smokers	0.95	0.87
Non-smokers	1.03	0.96

The discrepancy between the overall results and the stratified results is best explained by which of the following?

- A. Confounding (69%)
- B. Effect modification (17%)
- C. Measurement bias (5%)
- D. Meta-analysis (3%)
- E. Observer bias (2%)
- F. Recall bias (1%)

Omitted
Correct answer
A

69%
Answered correctly

01 sec
Time Spent

06/04/2020
Last Updated

Explanation

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Initial crude analysis confounded by smoking status

		Bladder cancer	
		Yes	No
Alcohol use	Yes	23	207
	No	26	444

RR = 1.81
p-value= 0.03

Stratified analysis removes confounding effects of smoking

Smokers

		Bladder cancer	
		Yes	No
Alcohol use	Yes	19	81
	No	14	56

RR = 0.95

Non-smokers

		Bladder cancer	
		Yes	No
Alcohol use	Yes	4	126
	No	12	388

RR = 1.03

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Stratified analysis removes confounding effects of smoking

Smokers

Alcohol use	Bladder cancer: Yes	Bladder cancer: No
Yes	19	81
No	14	56

RR = 0.95
p-value= 0.87

Non-smokers

Alcohol use	Bladder cancer: Yes	Bladder cancer: No
Yes	4	126
No	12	388

RR = 1.03
p-value= 0.96

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Confounding occurs when the exposure-disease relationship is muddled by the effect of a confounding variable, an extraneous factor associated with both exposure and disease. An example is shown in the exhibit. In a primary school, it may appear on crude analysis that students with bigger shoe sizes have a higher level of intelligence. However, this association is actually a result of age, not shoe size: Older students tend to have bigger shoe sizes and also to be more intelligent. Age is a confounder because it is associated with both shoe size and intelligence and muddles the association between them. When study subjects are grouped by age (**stratification**), the association between shoe size and intelligence is no longer significant.

Similarly, initial crude analysis suggested that alcohol use was associated with bladder carcinoma (similar to shoe size being associated with intelligence), with a relative risk (RR) of 1.81 and a p-value <0.05. However, smoking is associated with both bladder carcinoma and alcohol use. Therefore, **smoking** is a potential confounder that may explain the association observed between alcohol use and bladder cancer (similar to age in the school example). Stratified analysis by smoking status shows that both smokers and non-smokers have an RR ~1 with large p-values (>0.05). The RR of 1.81 found on crude analysis disappears and there is no true association between alcohol consumption and bladder cancer.

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(Choice B) Effect modification results when an external variable positively or negatively impacts the observed effect of a risk factor on disease status. When analysis is performed based on stratification by this external variable, there will be a significant difference in risk between the stratified groups. For instance, aspirin use is associated with Reye syndrome in children but not adults; therefore, age modifies the effect of aspirin on Reye syndrome development. Effect modification can easily be confused with confounding; but stratified analysis can help distinguish between them. With confounding, there is usually no significant difference between the strata (as in this case with the smoker and non-smoker strata).

(Choices C and E) Measurement bias and observer bias distort the strength of association by misclassifying exposed/unexposed and/or diseased/nondiseased subjects. The scenario does not describe any issues that could affect the classification process.

(Choice D) Meta-analysis refers to compiling results from several studies to increase analysis power.

(Choice F) Recall bias results from inaccurate recall of past exposure by people in the study and applies mostly to retrospective (eg, case-control) studies.

Educational objective:
Confounding occurs when the exposure-disease relationship is muddled by the effect of an extraneous factor associated with both exposure and disease. Confounding bias can result in the false association of an exposure with a disease.

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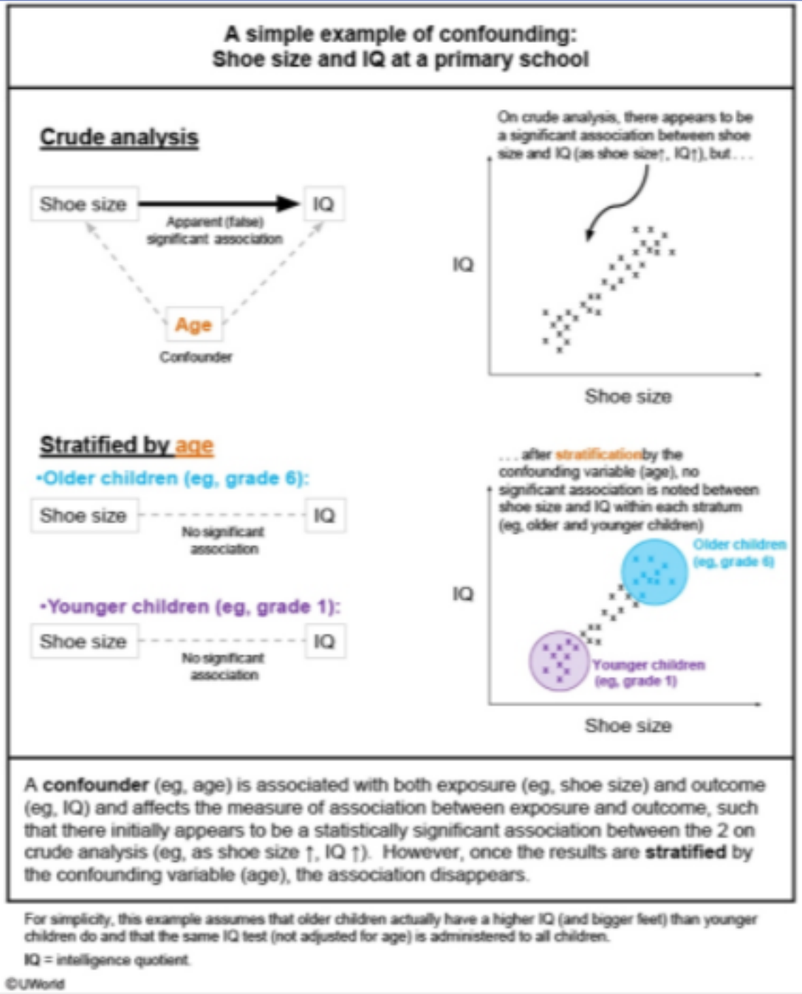
Confounding occurs when the exposure-disease relationship is muddled by the effect of a confounding variable, an extraneous factor associated

Exhibit Display



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Biostatistics	Biostatistics & Epidemiology	Confounding, effect modification, bias, errors
Subject	System	Topic

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A study evaluated the role of angiotensin-converting enzyme (ACE) inhibitors in the prevention of coronary events in patients with diabetes. During 5 years of follow-up, 120 out of 400 diabetic patients who had taken an ACE inhibitor developed an acute coronary event. Over the same time, 100 out of 300 diabetic patients who had not taken an ACE inhibitor experienced coronary events. What was the relative risk of developing a coronary event in diabetic patients who were taking ACE inhibitors compared to diabetic patients who were not taking ACE inhibitors?

A. (120x100)/(280x200)

B. (120x200)/(100x280)

C. (120x280)/(100x200)

D. (120/220)/(280/480)

E. (120/400)/(100/300)

Submit

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- A. (120x100)/(280x200) (3%)
- B. (120x200)/(100x280) (11%)
- C. (120x280)/(100x200) (4%)
- D. (120/220)/(280/480) (3%)
- ✓ E. (120/400)/(100/300) (77%)

Omitted
Correct answer
E

77%
Answered correctly

02 secs
Time Spent

02/04/2020
Last Updated

Explanation

It is important to know how to calculate some basic measures of association when given raw data. The first step is to organize the data into a 2×2 (contingency) table as shown below. The standard format includes the exposures in the rows (with "exposure present" listed above "exposure absent") and the outcomes in the columns (with "outcome present" listed before "outcome absent").

	Coronary event	No coronary event	
ACE inhibitor	120 (a)	280 (b)	400

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- ✓ E. (120/400)/(100/300) (77%)

Omitted
Correct answer
E

77%
Answered correctly

02 secs
Time Spent

02/04/2020
Last Updated

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	Coronary event	No coronary event	
ACE inhibitor	120 (a)	280 (b)	400
No ACE inhibitor	100 (c)	200 (d)	300
	220	480	700

The relative risk (RR) represents the risk of an outcome (eg, coronary event) in the exposed (eg, angiotensin-converting enzyme [ACE] inhibitor) divided by the risk of that outcome in the unexposed (eg, no ACE inhibitor). For cohort studies, it is calculated using the following formula:

RR = [a/(a+b)] / [c/(c+d)] = (120/400)/(100/300) = 0.90

Understanding the values calculated (rather than memorizing several formulas) would prevent errors that could occur if the standard format for the 2×2 table is not followed. By definition, RR = risk among the exposed/risk among the unexposed. In this example, 400 diabetic patients were taking ACE inhibitors (exposed) and 120 of those had a coronary event. Therefore, the risk among the exposed is 120/400. Similarly, 300 diabetic patients were not taking ACE inhibitors (unexposed) and 100 of those had a coronary event. Therefore, the risk among the unexposed is 100/300. The RR is the ratio of those 2 values: RR = (120/400)/(100/300).

(Choice B) The odds ratio (OR) is calculated using the following formula: OR = ad/bc. The OR is often calculated in case-control studies where RR cannot be obtained because such studies do not follow patients over time to determine the incidence of a new outcome.

Educational objective:
The relative risk (RR) represents the risk of an outcome in the exposed divided by the risk of that outcome in the unexposed. Applying the correct formula for RR calculations depends on the proper formatting of a 2×2 (contingency) table.

Biostatistics Biostatistics & Epidemiology Risk

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absent") and the outcome

The relative risk (RR) repr
divided by the risk of that

RR = [a/(a+b)] / [c/(c+d)] =

Understanding the values
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patients were not taking A
100/300. The RR is the ra

(Choice B) The odds rati
RR cannot be obtained be

Educational objective:
The relative risk (RR) repr
formula for RR calculation

Biostatistics Biostatistics & Epidemiology Risk

Exhibit Display

	Outcome/disease present	Outcome/disease absent	
Exposure/risk factor present	a	b	a + b
Exposure/risk factor absent	c	d	c + d
	a + c	b + d	

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A 45-year-old man comes to the office for a routine visit. The patient has a first-degree relative with Alzheimer dementia and is concerned about his chances of developing the disease. He has read in the newspaper that decreased consumption of yellow and orange fruits and vegetables has been associated with Alzheimer disease and would like to know how likely he is to develop the disease. A medical literature review uncovers a recent cohort study that evaluated the association between blood carotene concentration and Alzheimer disease. The development of the disease was evaluated in a 20-year follow-up study of 200 middle-aged subjects who have a first-degree relative with Alzheimer disease. The results are as follows:

	Low carotene level	Normal carotene level	Total
Developed Alzheimer disease	18	42	60
Did not develop Alzheimer disease	27	113	140
Total	45	155	200

Assuming the patient has low carotene levels, what is his 20-year risk of developing Alzheimer disease?

A. 0.19
B. 0.23
C. 0.27
D. 0.30
E. 0.40

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A. 0.19
B. 0.23
C. 0.27
D. 0.30
E. 0.40

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a recent cohort study that evaluated the association between blood carotene concentration and Alzheimer disease. The development of the disease was evaluated in a 20-year follow-up study of 200 middle-aged subjects who have a first-degree relative with Alzheimer disease. The results are as follows:

	Low carotene level	Normal carotene level	Total
Developed Alzheimer disease	18	42	60
Did not develop Alzheimer disease	27	113	140
Total	45	155	200

Assuming the patient has low carotene levels, what is his 20-year risk of developing Alzheimer disease?

A. 0.19 (3%)
B. 0.23 (3%)
C. 0.27 (4%)
D. 0.30 (15%)
✓ E. 0.40 (73%)

Omitted
Correct answer

73%
Answered correctly

05 secs
Time Spent

04/29/2020
Last Updated

Risk is the probability of developing a disease or other health outcome over the study period. In this example, it represents the probability of developing Alzheimer disease over a 20-year period among middle-aged subjects who have a first-degree relative with the disease. To calculate this probability in subjects with low carotene levels, divide the number of subjects who develop Alzheimer disease in the low carotene group (18) by the overall number of subjects in the low carotene group (18 + 27 = 45).

Risk of developing Alzheimer disease among subjects with low carotene = 18 / (18 + 27)
= 18 / 45 = **0.40**

This means that, among subjects with low carotene levels, there is a 40% probability of developing Alzheimer disease in 20 years.

Note that this is different from the **relative risk (RR)** of Alzheimer disease in subjects with low carotene levels compared to those with normal carotene groups:

RR = risk of developing Alzheimer disease among subjects with low carotene levels / risk of developing Alzheimer disease among subjects with normal carotene levels = 0.4 / [42 / (42 + 113)] = 0.4 / 0.27 = 1.48

As the data is not presented in the standard 2 × 2 (contingency) table format, care must be taken to perform the calculations without relying on memorized formulas.

(Choices A and D) The prevalence of low carotene (exposure) among subjects who do not develop Alzheimer disease is 27 / (27 + 113) = 27 / 140 = 0.19 (19%). The prevalence of low carotene (exposure) among subjects who develop Alzheimer disease is 18 / (18 + 42) = 18 / 60 = 0.3 (30%).

(Choice B) The prevalence of low carotene in the entire cohort is (18 + 27) / (18 + 42 + 27 + 113) = 45 / 200 = 0.23 (23%).

(Choice C) As noted in the RR calculation above, the 20-year risk of developing Alzheimer disease among subjects with normal carotene levels is 42 / (42 + 113) = 42 / 155 = 0.27 (27%).

Educational objective:
Risk is the probability of developing a disease over a certain period of time. To calculate this probability, divide the number of affected subjects by the total number of subjects in the corresponding exposure group.

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Exhibit Display

	Outcome/disease present	Outcome/disease absent	
Exposure/risk factor present	a	b	a + b
Exposure/risk factor absent	c	d	c + d
	a + c	b + d	

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This means that, among subjects with low carotene levels, there is a 40% probability of developing Alzheimer disease in 20 years.

Note that this is different from the **relative risk (RR)** of Alzheimer disease in subjects with low carotene levels compared to those with normal carotene groups:

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As the data is not presented in the standard 2 × 2 (contingency) table format, care must be taken to perform the calculations without relying on memorized formulas.

(Choices A and D) The prevalence of low carotene (exposure) among subjects who do not develop Alzheimer disease is 27 / (27 + 113) = 27 / 140 = 0.19 (19%). The prevalence of low carotene (exposure) among subjects who develop Alzheimer disease is 18 / (18 + 42) = 18 / 60 = 0.3 (30%).

(Choice B) The prevalence of low carotene in the entire cohort is (18 + 27) / (18 + 42 + 27 + 113) = 45 / 200 = 0.23 (23%).

(Choice C) As noted in the RR calculation above, the 20-year risk of developing Alzheimer disease among subjects with normal carotene levels is 42 / (42 + 113) = 42 / 155 = 0.27 (27%).

Educational objective:
Risk is the probability of developing a disease over a certain period of time. To calculate this probability, divide the number of affected subjects by the total number of subjects in the corresponding exposure group.

Biostatistics	Biostatistics & Epidemiology	Risk
Subject	System	Topic

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